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AN EXPERIMENTAL STUDY OF URETEROINTESTINAL IMPLANTATION

V. The Destiny of the Implanted Ureter

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EXPERIMENTAL investigation has yielded abundant proof that the lower portion of the implanted ureter constitutes an area of crucial importance in determining the success or failure of a ureterointestinal anastomosis. At successive stages following implantation of the dog's ureter by various modifications of the submucosal method, the animals either died or were killed and the intraluminal and intramural segments were subjected to a special study. In addition to gross and microscopic examination, the ureters in several specimens were injected with a 20 per cent suspension of India ink in gelatin and the region of the anastomosis was cleared by the Spalteholz-Skarda technique in order to localize areas of constriction or dilatation. These findings were correlated with the changes reflected in the upper urinary tract.

It was observed that healing at the site of the anastomosis takes place either by primary union and early epithelization or, in the presence of infection, by granulation, cicatrization and late epithelization (Table I). Although pure forms of both processes occur, the two are more usually associated in one of an innumerable number of possible relationships.

Immediately following operation the usual traumatic manifestations make their appearance. There is edema of the operative area with an infiltration of lymphocytes and plasma cells. Areas of hemorrhage may be present (Fig. 1). A foreign body reaction is observed in the region of the sutures.

If there is no infection or if only a mild degree of infection supervenes, as commonly observed in ureterovesical reimplantation, this reaction rapidly subsides and healing occurs by primary intention (Fig. 2). This is usually achieved by the sloughing of the intraluminal segment of the ureter. Only in rare instances is the length of this segment preserved exactly as introduced at operation. Most frequently a variable portion of the end separates so that the new orifice is in the plane of the mucosa of the implanted viscus or is situated on a low papilla.

In the absence of infection, sloughing is caused by anemic necrosis alone. The reaction is admirably demonstrated in a series of experiments in which a hollow catgut cylinder

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TABLE I.—FORMS OF HEALING FOLLOWING URETERAL IMPLANTATION

I. Early traumatic edema causing variable degrees of ureteral obstruction	
Without ↓ *Infection*	*With* ↓ *Infection*
II. Healing by primary union. Early epithelization.	II. Infection: Acute, subacute to chronic. Early obstruction of the ureter. Healing by granulation.
III. Healing completed without cicatrization. Final relief of temporary obstruction. (The end of the ureter may slough from anemic necrosis)	III. Cicatrization: Formation of scar tissue may give rise to late obstruction of the ureter. Late epithelization. (The end of the ureter may slough from infectious gangrene)

was placed in the lumen of the end of the ureter in an attempt to assure the patency of the anastomosis. Since the cylinders fit snugly, in many instances, with the occurrence of edema, the blood vessels became obliterated and necrosis from pressure ensued (Fig. 3).

If healing takes place by primary union, there is little constriction of the ureter other than that occasioned by the transient operative edema. Free communication as demonstrated by injections of gelatin is illustrated in Figures 4 and 5. In addition to exemplifying the ideal which is striven for in all implantations, these models serve for comparison with specimens showing obstruction.

When a severe degree of infection ensues, an entirely different picture is presented. Soon after the onset of edema, the entire wall of the redundant end of ureter becomes engorged with leucocytes, chiefly of the polymorphonuclear strain. The adventitia is invaded first but the process soon spreads through the muscularis, the submucosa, and to a lesser degree into the mucosa. The surface of the stump is encased in an inflammatory débris containing conglomerations of bacteria (Fig. 6). The more fulminating the inflammatory reaction, the greater is the tendency to occlude the lumen of the ureter. Granulation tissue makes its appearance and gradually replaces the exudate. New capillaries are formed and, as they grow into the granulations, fibroblasts appear (Fig. 6 b). Cicatrization becomes greatest in the adventitia and portions of the muscularis where the muscular fibers are destroyed. As healing progresses the inflammatory process recedes from the acute to the subacute, and finally to the chronic stage. The scar tissue contracts over a period of weeks and months to produce, as a general rule, a permanent stricture of the ureter (Fig. 7). Healing is prolonged and epithelization is delayed.

Though the end of the ureter is first to be invaded, its intramural extent and the adjacent parts of the intestine do not escape the inflammatory process. Infection spreads upward along the path of the ureter into the intermuscular planes and submucosa of the intestine. The mucosa itself shows minimal invasion, probably because of a natural immunity to the fecal content. Sutures form rallying points for infection, and abscesses are prone to develop about them (Fig. 8). Areas of inflammation outside the ureter do not compress it. Except for constrictions and angulations caused by sutures which are placed improperly, obstruction to the ureter is always produced by changes within its own wall.

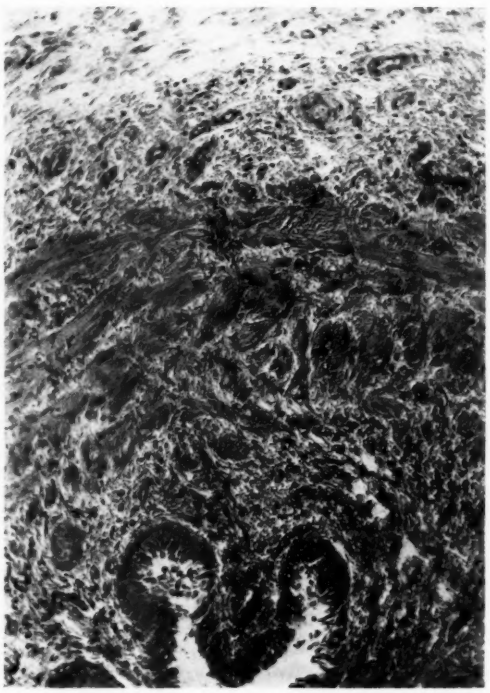


Fig. 1. The early traumatic manifestations seen in the intraluminal end of the ureter 2 days following ureterointestinal anastomosis. There are areas of hemorrhage best seen in the submucosa and diffuse edema with an infiltration of lymphocytes and plasma cells throughout all layers.

The end of the ureter sloughs more frequently in the presence of infection than from anemic necrosis alone. As cellulitis progresses, blood vessels and lymphatics become occluded, infectious gangrene results, and separation occurs at the point where sufficient vascularization ends. The greater part of this slough usually takes place soon after the first week, but it may be delayed for a month or more. Despite its own vulnerability to infection, the intestine gives the appearance of forming a protective covering around the submucosal course of the ureter, for, although it is common for a fulminating ureteritis to extend up to the place where the ureter enters the wall of the intestine, such a generalized infection rarely extends beyond it. The end often sloughs level with the rectal mucosa, but not proximal to this point, except in instances of massive necrosis, as will be described. A cross circulation from the intestine lends added vitality to the ureter soon after the first week.

The effects of these pathological changes upon the lumen of the ureter were observed following injection with gelatin. In localizing areas of obstruction, it is important not only to note a diminution in the normal caliber of the lumen but equally valuable to observe substantiating evidence from the effects of back-pressure on the kidney and ureter proximal to an area of suspected narrowing. Taking cognizance of both these features it was discovered that, in acute ureteritis, the lumen of the entire intraluminal segment is usually compressed. Later the very tip of the implanted ureter is the initial and most frequent site for the development of a stricture (Fig. 9). If more scar tissue is formed, the area of constriction involves the remainder of the intraluminal portion (Fig. 10). It is unusual for the process to advance into the intramural segment although this sometimes occurred after a period of several months (Fig. 11).

The question naturally arises as to how obstruction in the end of the ureter may be avoided. We have shown that the reduction of infection in the field of implantation (1) is conducive to the prevention of ureteritis with its attendant stasis and later formation of stricture.

We attempted to evaluate, as another factor, the relative advantages of implanting a long or a short end of ureter at operation. In an experimental series of ureterointestinal anastomoses, an end less than 1 centimeter in length was utilized on one side, while the end

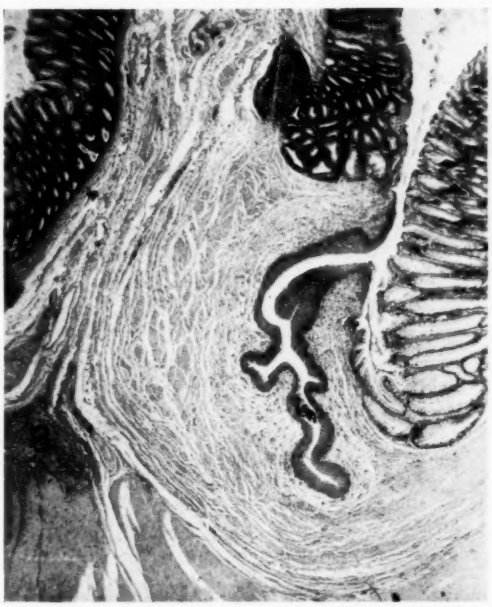


Fig. 2. Ureterointestinal orifice following healing by primary union. Note the perfect fusion of the ureteral with the rectal mucosa and the coaptation of the two musculatures. *a*, Shows a foreign body reaction in the region of a suture.

Fig. 3. Anemic necrosis of the intraluminal segment of the ureter caused by the pressure of a catgut cylinder, 2 days following ureterointestinal anastomosis. The ureter is seen as only a ghost of its normal structure. The catgut cylinder lies within the lumen.

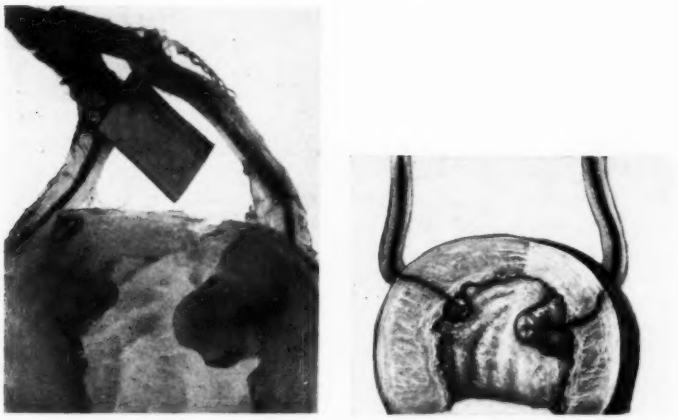


Fig. 4. Ideal ureterovesical communication 5 weeks following bilateral ureterocystoneostomy. There is no constriction of either ureter. A small papilla remains on the right, a long papilla on the left. The kidneys and ureters above are normal.

of the opposite ureter was left 3 centimeters long. Although an accurate statistical analysis of this factor was precluded by the complexity of other considerations, we concluded that the shortest possible end which is technically feasible is the most desirable. Since the intraluminal segment bears the brunt of the inflammatory reaction and is the area most consistently narrowed by acute inflammation, as well as by the later formation of stricture, it seems rational to reduce its dimensions to an absolute minimum. Furthermore, the exposed surfaces of the adventitia unprotected by mucosa or by the wall of the intestine afford the best possible foothold for the entrance of infection.

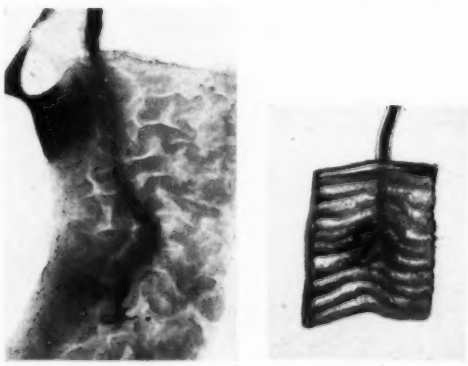


Fig. 5. Ideal ureterointestinal communication 6 weeks following a right submucosal transplant. There is no constriction or dilatation of the ureter. The upper urinary tract is normal.

We have found that our best results are obtained by dividing the end of the ureter tangentially and carrying a longitudinal incision a short distance beyond. Starting at the most proximal point of the beveled end, the wall is divided longitudinally almost to the level at which it is to emerge from the intestine. This step reduces the possibility of occlusion which, as we have demonstrated, is so likely to occur in a long, redundant end and brings the new orifice close to the protected intramural portion of the ureter. Furthermore, it opens a broad expanse of ureteral mucosa to promote fusion with that of the intestine.

In our experience, the Coffey No. 3, Higgins method and other operations depending on a transfixion suture for the establishment of an orifice are complicated by a higher incidence of obstruction and ascending infection. There is a tendency for the minute orifice to contract from cicatrization and, in a few instances, complete occlusion has occurred. The temporary period of absolute ureteral obstruction is a serious disadvantage of the Coffey No. 3 procedure. One inherent danger of any method which incorporates a transfixion suture is the possibility that the suture may fail to slough through.

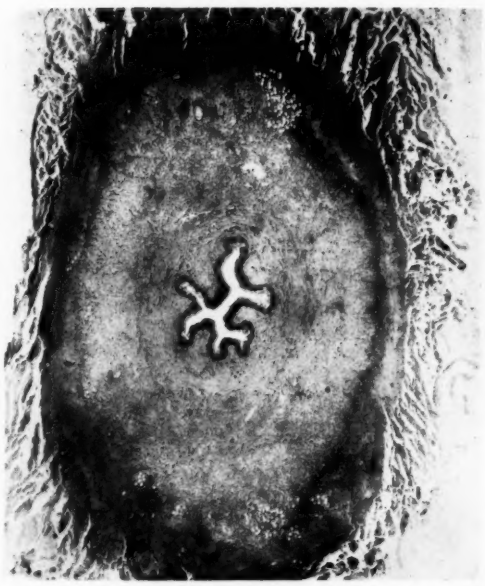
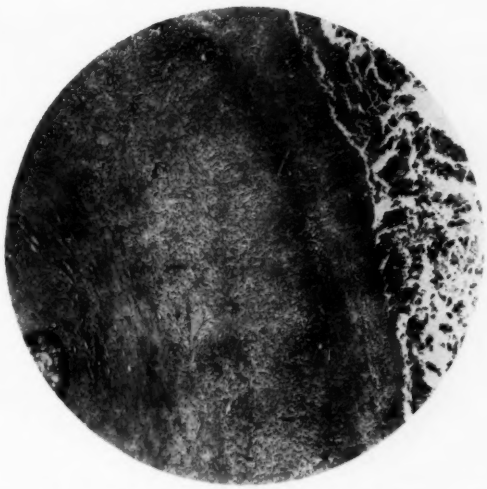


Fig. 6. Acute inflammatory reaction involving the stump of the implanted ureter 1 week following ureterointestinal anastomosis. Leucocytes chiefly of the polymorphonuclear



strain are seen in all layers. The surface of the stump is encased in an inflammatory débris containing conglomerations of bacteria, best seen as dark areas in the high power photomicrograph, right. This view likewise shows the formation of granulation tissue, evidenced as fibroblasts and new capillaries in a zone surrounding the muscularis. Note the formation of cysts in the mucosa as a result of inflammation.

Transplantation of the ureter is possible only because the blood supply derived from the upper and middle portions is adequate to nourish its entire length. Since some vessels course through the adventitia, care must be

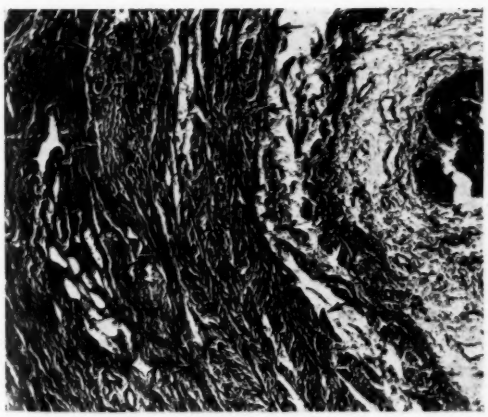


Fig. 7. Stricture of the intraluminal segment of the ureter 6 weeks following submucosal ureterointestinal implantation. The arrows indicate the marked atrophy and replacement of the muscularis by scar tissue as demonstrated by connective tissue stain. (The gross specimen is illustrated in Fig. 10.)

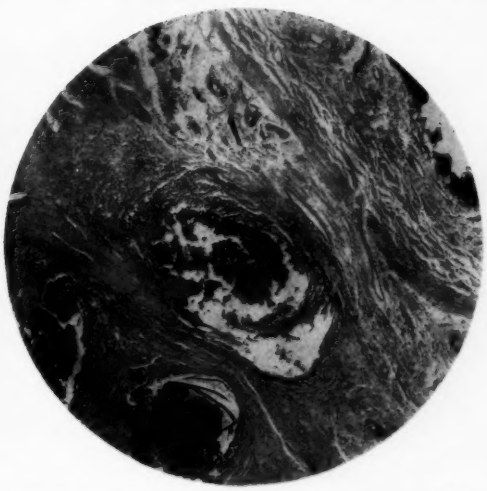


Fig. 8. Acute ureteritis in the intramural segment of the ureter 18 days following ureterointestinal anastomosis. Note how silk sutures form rallying points for the formation of abscesses.

Fig. 9a.

Fig. 9b.

Fig. 10a.

Fig. 10b.

Fig. 11.

Fig. 9. Marked constriction at the ureterointestinal orifice which opens on a small papilla. The intraluminal and intramural portions are widely dilated and marked hydroureter and hydronephrosis are present. The specimen is from a dog killed 1 month following a left submucosal ureterointestinal anastomosis.

Fig. 10. Constriction of the intraluminal segment of the ureter causing wide dilatation of the intramural portion and a marked hydroureter and hydronephrosis above. The specimen is from a dog killed 6 weeks after a right submucosal ureterointestinal anastomosis.

Fig. 11. Constriction of the intraluminal and intramural portions of the ureter, giving rise to a bilateral infected hydroureter and hydronephrosis above. The specimen is from a dog killed 4 months after a bilateral submucosal ureterointestinal anastomosis.

taken not to denude the ureter too completely preparatory to an anastomosis. Occasionally the blood supply is so completely destroyed that an anemic necrosis of the ureter reaches above the site of implantation. When this occurs, leakage is inevitable and peritonitis ensues. Infectious gangrene giving rise to a massive necrosis may produce the same result. The danger of this complication is likewise increased by injury to the blood supply (Figs. 12 and 13).

In some of the operations the peritoneum covering the lower portion of the ureter was dissected with the ureter and used as a cuff around it in implanting the end into the bowel. This has been recommended as a measure to assure the preservation of an adequate blood supply. At necropsy, however, we noted no decrease in the incidence of infection and obstruction in the ends of the ureters so treated. Ureteritis and sloughing of the ends occurred as usual, with the peritoneum participating in the process.

A pathological characteristic which sometimes plays a part in shaping the final result is the adhesive quality of inflamed surfaces. This is displayed by the specimen illustrated in Figure 14. Two long ends of ureter which

Fig. 12. Infectious gangrene involving the intramural segment of the ureter 3 days after a right submucosal implantation with the use of a catgut cylinder.

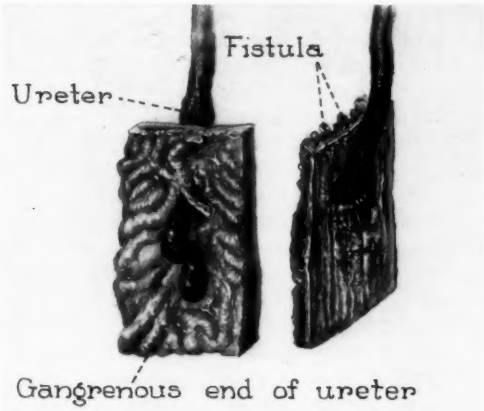


Fig. 13. Infectious gangrene of implanted ureter extending 2 centimeters above the site of anastomosis. The dog succumbed, 5 days after a right ureterointestinal implantation, to peritonitis caused by leakage around the ureter and a fistula in the ureter itself.

had been implanted into the rectum came into contact and, incident to the infectious process, became fused into an inseparable mass. A similar fusion giving rise to more disastrous consequences, was occasionally noted within the lumen of the ureter, sealing it shut at the place where it had been crushed by a ligature in our first application of the divisible carrier (Fig. 15). In most instances the lumen became re-established, but in a few it remained permanently occluded. In still others an orifice at the side was formed at some point proximal to the tip. To prevent these complications, as mentioned previously, we now divide the end of the ureter tangentially, slit it longitudinally for a short distance beyond, and affix the divisible carrier to its very tip. Urinary contamination is prevented during this stage

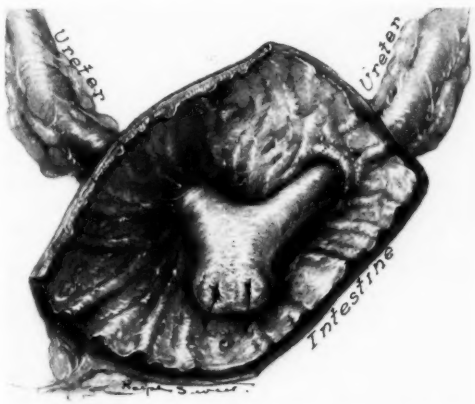


Fig. 14. Ureteritis adhesiva. Two long ends of ureter which were implanted into the rectum came into contact and, incident to the infectious process, became fused into an inseparable mass. The specimen is from a dog killed 2 months after a bilateral submucosal ureterointestinal anastomosis.

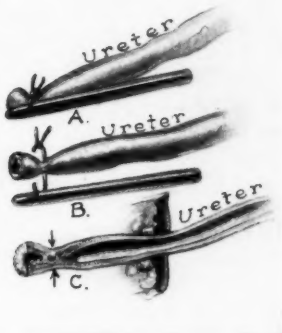


Fig. 15. Diagram illustrating how crushing the end of the ureter by a ligature during operation may lead to an adhesive process within the lumen and give rise to partial obstruction, or even to occlusion.

of the operation by temporary occlusion of the ureter with a bull-dog clamp. Gentle handling is important in order to minimize trauma with its resultant necrosis and infection.

We have demonstrated that ureteral obstruction and ascending infection following ureterointestinal anastomosis are attributable to the highly contaminated nature of the contents of the large intestine (1). In this paper we have traced the pathological changes which occur in the implanted ureter and have shown that the end of the implanted ureter is a region of crucial importance as concerns a successful result. Subsequent communications will be devoted, first, to the effect of these changes upon the upper urinary tract, especially to the relationship between ascending infection and ureteral obstruction (2) and, secondly, to the methods of reducing the infectious changes of the implanted portion so that primary healing of the end of the ureter will occur (3).

SUMMARY

The end of the implanted ureter constitutes an area of crucial importance in determining the success or failure of a ureterointestinal anastomosis. The pathological changes which occur in this structure are carefully traced, especially with a view to demonstrating the hazards which accompany damage to the blood supply and the entrance of infection; if extending above the site of the anastomosis, either anemic necrosis or infectious gangrene gives rise to fatal peritonitis. A virulent infection in the ureteral stump causes serious damage to the upper urinary tract first by acute ureteritis with its attendant stasis and later by the formation of stricture. The changes in the end of the ureter, therefore, play a great part in accounting for the morbidity and mortality, both early and late, which attend the operation.

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EXCISION OF THE HEAD OF THE PANCREAS FOR CARCINOMA WITH STUDIES OF ITS BLOOD SUPPLY

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DURING the past 15 years many advances have been made in the surgical treatment of carcinoma of the ampullary region of the duodenum. By far the greatest number of cases of obstructive jaundice due to this cause have been treated by a palliative type of operation in which the gall bladder or common duct has been anastomosed to the stomach or duodenum. It is remarkable that so few attempts at excision of carcinoma localized to this region have been attempted when one realizes that the first operation of this type was done as long ago as 1900 by Halsted. Up to 1927 Cohen and Colp were able to collect only 59 cases in which local excision of carcinoma of the ampulla was accomplished and, though only a relatively small number of these patients survived the operation more than a few days, there were 4 patients who lived beyond 18 months. This report apparently stimulated many surgeons to do the local excision type of operation, so that by 1935 Whipple, Parsons, and Mullins (16) were able to add 20 reported cases to those collected by Cohen and Colp, and in the same year Hunt and Budd found in the literature a total of 76 cases which had been treated in this manner.

Up to this time the lesion had been excised locally with, in the majority of cases, reimplantation of the bile duct; and in 1932 Walters first suggested that the immediate mortality rate from the operation could be reduced if it were preceded by a cholecystostomy. Whipple, Parsons, and Mullins, in their report in 1935, suggested a wide excision of the adjacent pancreas and duodenum for the first time, thus sacrificing the external secretion of this gland and substituting a gastroenterostomy in place of any attempt to preserve the duodenum. This proposed change was based on the following facts: (1) For many years it had been realized that the external secretion of the pancreas was not essential to life in animals, and it was thought that one could sacrifice it in man without ill effects. (2) A great many postoperative deaths from local excision of the ampulla were due to leakage of pancreatic secretion around the anastomosis which, of necessity, was formed between the amputated ends of the ducts and the duodenum. (3) Whipple stressed that the operation of wide excision, sacrificing the external secretion of the pancreas, conformed to the main principle of cancer surgery in excising large blocks of tissue wide of the growth. This last consideration is of extreme importance, for many cases will show extension into the wall of the common duct itself or the adjacent pancreas, and there is really no point in attempting to excise these lesions if one does not seriously attempt to remove all cancer tissue.

Since this more radical excision is much more time-consuming and involves more risk of shock to the patient who is already in a precarious position as a result of long-standing complete obstruction of the lower end of the bile duct, and in many cases of the pancreatic ducts, Whipple suggested that the operation be done in two stages. The first stage involved a cholecystgastrostomy and gastroenterostomy followed 4 to 6 weeks later by a wide excision of the lesion, a major portion of the duodenum being sacrificed and the previous gastroenterostomy relied on for re-establishment of the continuity of the gastrointestinal tract (Fig. 1).

Following this momentous contribution to the surgery of this region, numerous reports have appeared in the literature attesting to its sound principles and success. In 1938 Whipple (15) again made an important suggestion when he advocated a further change in the technique of the first stage because the cholecystgastrostomy had been found to possess certain defects. The fundamental principle of

Presented at the meeting of the Society of Clinical Surgery, Rochester, New York, May 16, 1941.

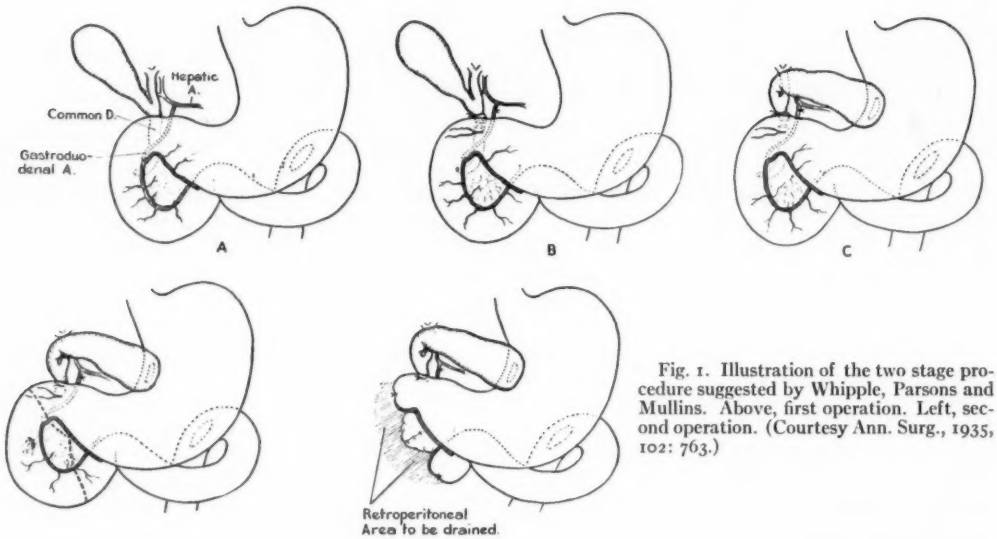

Fig. 1. Illustration of the two stage procedure suggested by Whipple, Parsons and Mullins. Above, first operation. Left, second operation. (Courtesy Ann. Surg., 1935, 102: 763.)

radical excision *en bloc* of the tumor by means of a two stage procedure remained unchanged. However, he was disturbed by numerous instances in which recurring cholangitis and hepatitis followed the first stage in spite of the provision of a large stoma between the gall bladder and the stomach. It was apparent by this time that the lack of pancreatic secretion did not interfere with the patient's nutrition; in fact, most of the patients constantly showed a gain in weight following the first stage of the operation. He proposed, therefore, a cholecystjejunostomy on the Roux principle, as shown in the accompanying diagram (Fig. 2), and reported 3 cases, none of which had been followed by cholangitis.

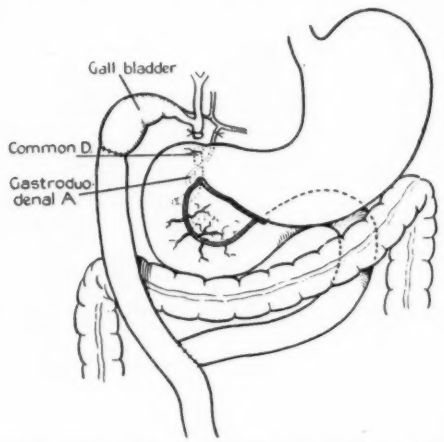

Fig. 2. Illustration of the change in the first stage operation to that of a cholecystojejunostomy on the Roux principle as suggested by Whipple. (Courtesy *Am. J. Surg.*, 1938, 40: 261.)

One point which should be borne in mind is that the mesentery of that portion of the jejunum forming the anastomosis with the gall bladder should be sutured to the parietal peritoneum at a considerable distance from the duodenum in order that the division of the peritoneum along the lateral border of the duodenum, at the second operation, can be accomplished without interfering with this leaf of mesentery. Furthermore, although Whipple recommends the ligation of the common duct just below the entrance of the cystic duct at the first operation, it is suggested that the common duct be left undisturbed so that one will not be hampered at the second operation by the presence of many adhesions in this region. If, however, the common duct has been opened for exploration during the first stage of the operation, it probably is wise to ligate it and leave a long silk suture for a marker, as he suggests.

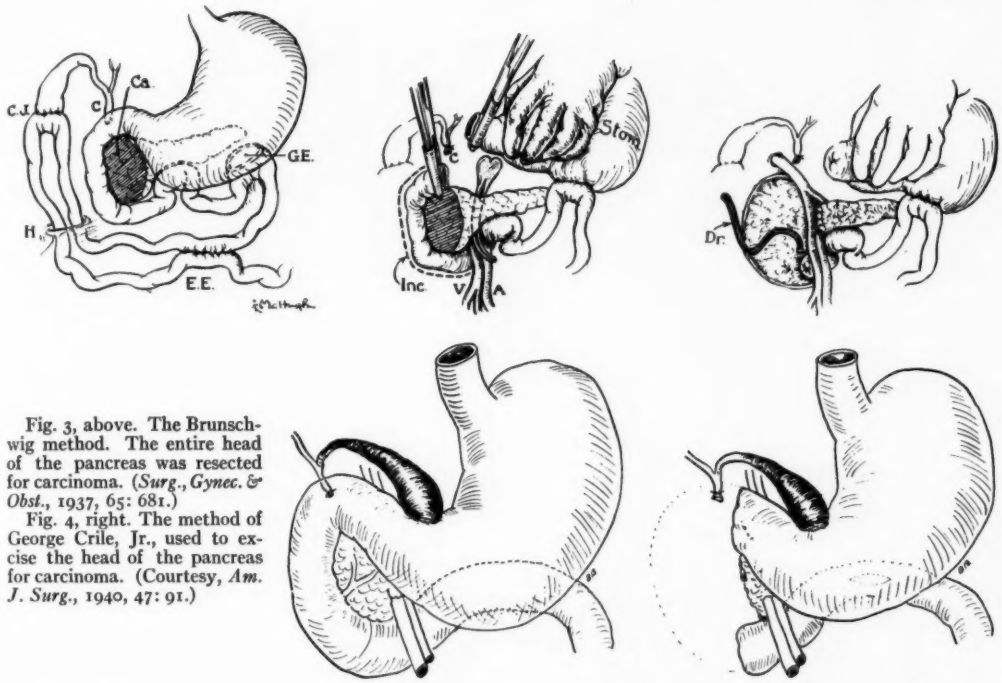

Fig. 3, above. The Brunschwig method. The entire head of the pancreas was resected for carcinoma. (*Surg., Gynec. & Obst.*, 1937, 65: 681.)

Fig. 4, right. The method of George Crile, Jr., used to excise the head of the pancreas for carcinoma. (Courtesy, *Am. J. Surg.*, 1940, 47: 91.)

Since Whipple's report, the use of vitamin K has disposed of the hazard of uncontrollable bleeding in patients of this type who are deeply jaundiced, and we believe it is quite possible, in patients who are otherwise in good condition, to accomplish this whole surgical procedure in one stage. In fact, in an article published this year, Kauer and Glenn have advocated that the problem be attacked with this in mind. In this clinic last year for the first time, Dr. Mahoney did a one stage operation for carcinoma of the ampulla of Vater with excellent results. However, the attempt to accomplish the operation in one stage requires a patient in excellent condition, extreme surgical speed and skill, and the provision during the operation of large amounts of plasma and blood to combat the surgical shock which would otherwise develop during such a long procedure.

Following all this very interesting work on the surgical treatment of carcinoma of the ampulla of Vater, a tremendous advance was made in 1937 when Brunschwig operated on a patient for carcinoma of the head of the pancreas in a two stage procedure and excised the entire head of the organ. Just previous to this, Lahey had recommended cholecystenterostomy rather than cholecystgastrostomy as a first stage, and Brunschwig made use of this in a rather unusual fashion (Fig. 3).

In the same year George Crile, Jr. reported another case of excision of the head of the pancreas for carcinoma, using a cholecystgastrostomy as the first stage, but, from the drawings presented, it would appear that the entire head was not excised (Fig. 4). It has occurred to us that excision of the entire head for carcinoma of the lower end of the bile duct and ampulla is possibly as easy as the removal of a wedge-shaped section of pancreas, for this must involve the time-consuming ligation of innumerable small vessels, whereas, as will be shown, only two main arteries require ligation if the entire head of this organ is excised. This procedure will also conform more to the general principle of wide excision of tissue beyond the local area of tumor growth.

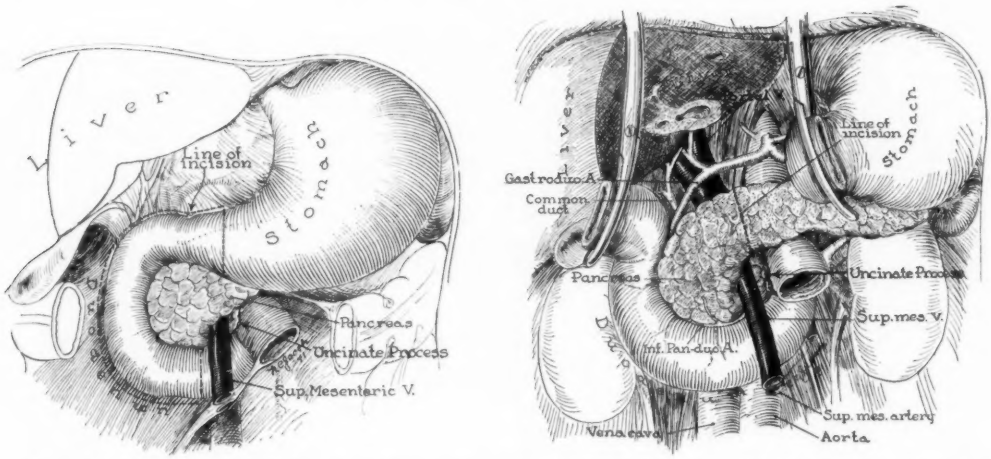

Fig. 5. a, left, The area of duodenum and pancreas to be excised outlined by the dotted line. b, Exposure after the division of the pylorus. The dotted line indicates the line of incision through the neck of the pancreas.

OPERATIVE PROCEDURE

Last year I attempted an operation for excision of carcinoma of the head of the pancreas which presented several interesting problems. The first stage of this operation required a choledochojejunostomy due to the fact that the patient possessed a nonpatent cystic duct and a small, scarred gall bladder which could not be utilized in a short-circuiting operation. Unfortunately this contributed to the patient's death following the second stage due to a separation of the suture lines as a result of traction on this region and consequent leakage of bile.

The second stage of the operation, as described by Brunschwig, is illustrated by Figures 5, 6 and 7. A transverse incision is employed to open the abdomen and silk sutures

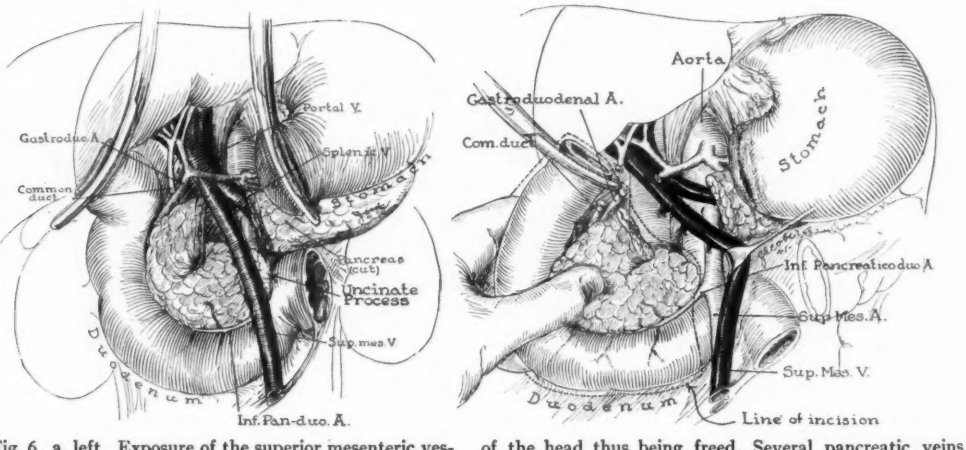

Fig. 6. a, left, Exposure of the superior mesenteric vessels by division of the neck of the pancreas and the projection of the uncinate process behind and medial to these vessels. b, Retraction of the head of the pancreas laterally and the mesenteric vein medially, the uncinate process of the head thus being freed. Several pancreatic veins have been ligated, as have the gastroduodenal artery and the common bile duct. The so-called normal origin of the inferior pancreaticoduodenal artery is shown in this drawing.

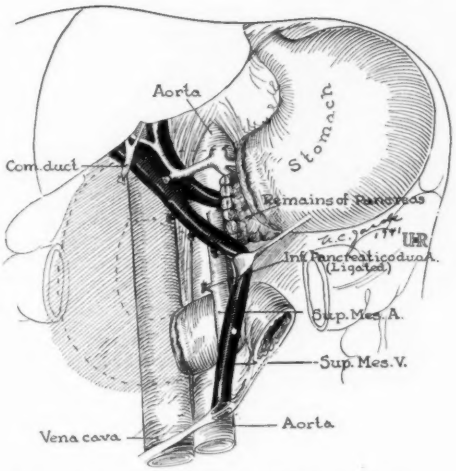

Fig. 7. The completed operation with gastroenterostomy not shown.

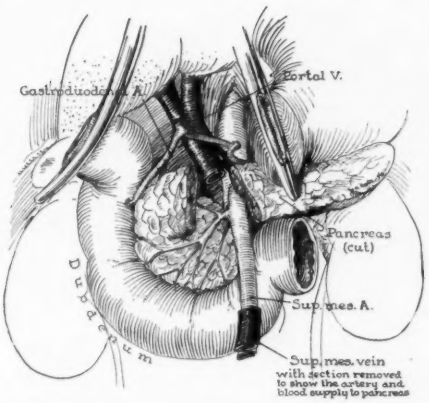

Fig. 8. Portion of the superior mesenteric vein has been removed to show the high origin and fan-shaped distribution of the inferior pancreaticoduodenal artery.

are used throughout. The pylorus is first divided and this immediately exposes the pancreas where a blunt instrument can be passed beneath the neck of the gland. Caution must be used to keep the instrument in close proximity to the deep surface of the gland for several important large vessels lie immediately behind it. The neck is then divided along the line shown in Fig. 5b. We used the actual cautery for this division feeling that bleeding would thereby be better controlled and the danger of leakage of pancreatic secretion decreased. However, Tripodi and Sherwin, in recent experiments on excision of the pancreas in dogs, have shown that the stump of the pancreas heals equally well and shows no tendency toward leakage of its external secretion whether one uses the scalpel, actual cautery, or high frequency knife. It probably would be safer to make the division with the scalpel, since there is actually very little bleeding from this portion of the pancreas and one could then more easily identify and ligate the main pancreatic duct issuing from the body of the gland. The first part of the duodenum is then mobilized from above, no attempt being made to separate it from the pancreas, and in the course of this part of the dissection the gastroduodenal artery and common bile duct are ligated and divided.

By dividing the pancreas at this point one immediately exposes the splenic and superior mesenteric veins where they join to form the portal vein, and it will be seen that the latter crosses the head of the pancreas in an oblique fashion, the superior mesenteric artery lying behind and hidden by the vein (Fig. 6a). Numerous small veins issuing from the head of the pancreas enter the superior mesenteric vein on its pancreatic surface, and these must be ligated while the vein is gently retracted medially in order to expose the upper and medial margins of the head as shown in Figure 6b. From this point on in the operation we

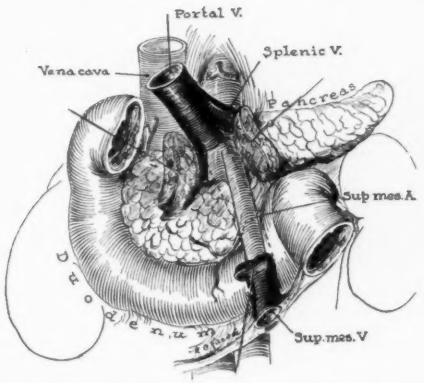

Fig. 9. Depicting the usual origin, course, and distribution of the inferior pancreaticoduodenal artery described in most textbooks of surgery and anatomy.

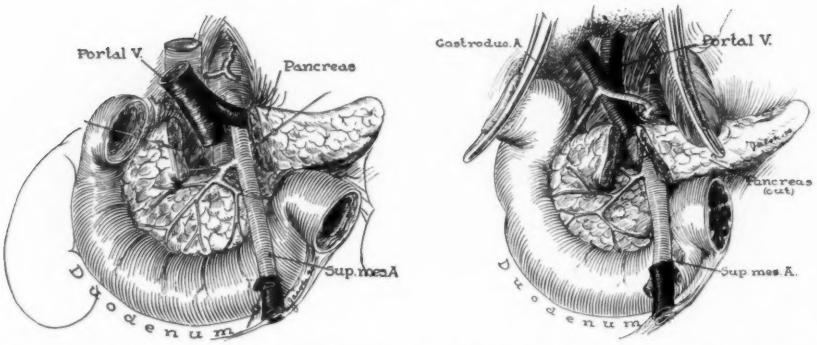

Fig. 10. a, left and b. Twelve of the 24 dissections studied revealed a high origin of the inferior pancreaticoduodenal artery, as shown. (A section of the superior mesenteric vein was removed to clarify the picture.)

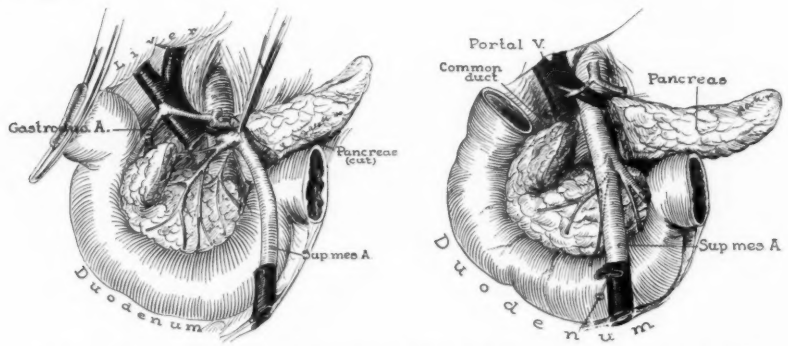

Fig. 11. a, left and b. A high posterior origin of the inferior pancreaticoduodenal artery.

encountered several interesting and unexpected difficulties. The duodenum has been mobilized by division of the lateral reflexion of peritoneum, and by blunt dissection the hand can be placed behind the duodenum and head of the pancreas where these structures lie immediately adjacent to the vena cava and aorta. In order to carry the dissection around the medial border of the head, it is necessary to provide some traction to free the uncinate process from its position beneath the superior mesenteric artery. When this maneuver was attempted in our patient he immediately developed a profound state of shock which persisted until the close of the operation and for 2 to 3 hours afterward in spite of all the usual methods which were used to combat it. We believe that this was due to the fact that the head of the pancreas is abundantly supplied with sympathetic nerves issuing in a radiating fashion from the plexus around the root of the superior mesenteric artery. In a good many cases this traction can be avoided, but it is suggested that, in order to prevent this sympathetic reflex from operating, one should inject the region of the plexus with novocain as soon as the neck of the pancreas has been divided.

The next problem which we encountered was that the inferior pancreaticoduodenal artery does not always arise low on the superior mesenteric artery and proceed laterally in the interval between the pancreas and duodenum as described in most textbooks of surgery and anatomy. In the case under discussion, it had its origin high up near the root of the artery and proceeded downward and outward, as shown in Figure 8. This caused us some concern, inasmuch as we were doubtful whether or

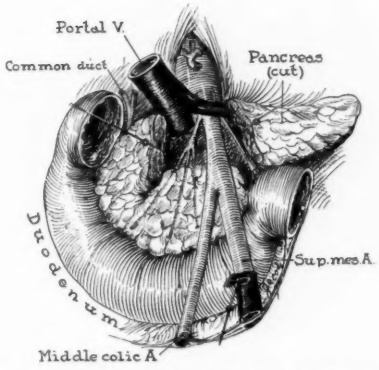

Fig. 12. Another case of high origin of the inferior pancreaticoduodenal artery and the only case in which its branches reached the pancreas and duodenum on its posterior aspect.

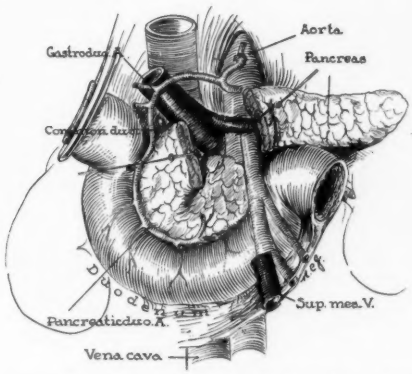

Fig. 13. The only case in the group in which no inferior pancreaticoduodenal artery was present.

not this vessel could be ligated at its origin without endangering the vitality of the third portion of the duodenum at that point where we intended to amputate it and turn in the distal end. We felt that primary ligation of this vessel and the gastroduodenal artery as early as possible in the operation would render the resection relatively bloodless and conserve much time otherwise occupied in the ligation of numerous small bleeding points. The operation should be completed by inverting the stump of remaining duodenum, closing the stump of the body of the pancreas with three or four silk mattress sutures and the provision of a posterior gastroenterostomy as shown in Figure 7. Our patient, however, was in such a severe stage of shock that we saved some time by sewing the stump of the duodenum to the distal end of the stomach. In the future it would be better to do the gastroenterostomy as the first step in the second stage rather than be faced with this at the close of the operation. Shock, if it develops at all, is most likely to occur when one uses traction on the head of the pancreas, and one should be in a position to close the abdomen at once. In our case this was accomplished with through-and-through wire sutures without drainage. The patient died 3 days later of bile peritonitis due to a leakage from the previous choledochojejunostomy and a complete thrombosis of the portal vein and its tributaries. I cannot explain the development of the portal thrombosis and it is regrettable that it occurred, for there was a concomitant gangrene of the stomach and jejunum so that we were unable to determine whether or not the ligation of the inferior pancreaticoduodenal artery interfered with the vitality of the duodenal stump.

STUDIES OF THE BLOOD SUPPLY OF THE HEAD OF THE PANCREAS AND DUODENUM

The finding of the high origin of the inferior pancreaticoduodenal artery led to an anatomical investigation of the blood supply of the head of the pancreas with particular reference to this artery. With the co-operation of Dr. W. B. Hawkins in the department of pathology and Prof. Karl Mason in the department of anatomy, 24 dissections were carried out, in each instance the operative approach described above being used; examples of these are illustrated by Figures 9 to 16. In only 8 of the subjects were we able to demonstrate the normal textbook picture of the artery as depicted in Figure 9. In 12 instances, comprising half of the subjects studied, the artery arose from a high position on the superior mesenteric, frequently from its posterior aspect (Figs. 10a, b and 11a, b). The artery immediately breaks up into many smaller vessels which proceed in a fan-shaped distribution to the anterior surface of the pancreas and third portion of the duodenum. Figure 12 reveals a very high origin of the artery and is the only instance in which its branches reached the

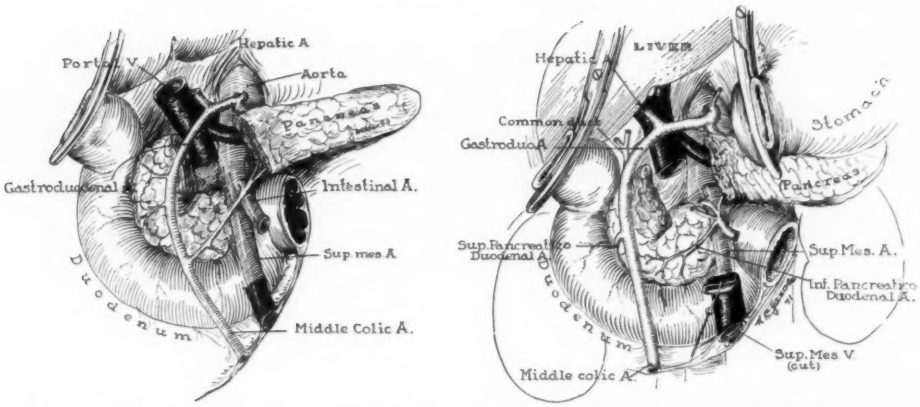

Fig. 14. a, left, and b. The abnormal origin of the middle colic artery from the gastroduodenal artery.

head on the posterior surface. This subject also presented a very high origin of the middle colic artery which then pursued a course across the duodenum at the point where it would be turned in during the operation. Further dissection of this group of high origins of the inferior pancreaticoduodenal artery revealed that, as a general rule, the first intestinal branch arose from the posterior surface of the superior mesenteric artery above the duodenum and supplied the terminal portion. In these cases, therefore, there probably exists an adequate blood supply to that portion of the duodenum which would be transected and turned in during the operation in spite of the high ligation of the inferior pancreaticoduodenal artery at its point of origin.

One dissection revealed no vessel corresponding to the inferior pancreaticoduodenal (Fig. 13). The 3 subjects, illustrated by Figs. 14a, b and 15, show a most unusual and unsuspected anomaly. In 2 of these the middle colic artery has arisen as a main branch from the gastroduodenal. In such a case, it can be readily seen that ligation of the gastroduodenal artery early in the operation, as suggested, before discovery of this anomaly might result in a serious impairment of the arterial supply of the transverse colon. With the exception of this anomaly the early ligation of the gastro-

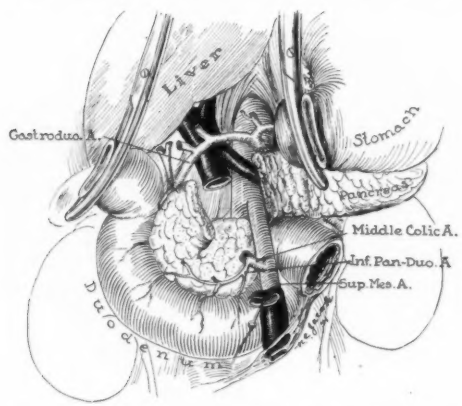

Fig. 15. In this case the inferior pancreaticoduodenal artery arose from the middle colic artery.

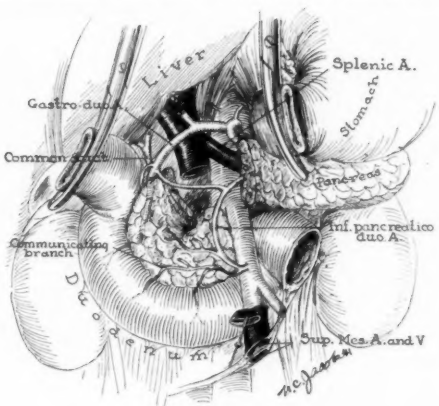

Fig. 16. Normal origin of inferior pancreaticoduodenal artery. Many anastomotic vessels supply the pancreas.

duodenal artery at its origin is possible in the operative technique described, for it was remarkably constant in its origin, course, and distribution in all 24 dissections. In the other case (Fig. 15) the inferior pancreaticoduodenal artery is a branch from the middle colic, and here again an unfortunate arterial ligation would be possible. Figure 16 demonstrates a very peculiar arrangement of aberrant vessels forming a perplexing anastomosis on the anterior surface of the pancreas

SUMMARY

1. A case is presented in which a two stage resection of the entire head of the pancreas for carcinoma was accomplished, and it is recommended that the first stage be that of a cholecystjejunostomy following the Roux principle as advocated by Whipple.

2. The actual excision of the entire head of the pancreas, rather than a partial wedge excision, together with the major portion of the duodenum, is feasible and can be greatly facilitated by ligating the gastroduodenal artery and the inferior pancreaticoduodenal artery early in the operation; thus the greater portion of the dissection is rendered relatively bloodless.

3. However, as a result of 24 dissections in which the various stages of the operation were carried out according to plan, certain marked deviations from the normal distribution of these vessels, as described in most textbooks of anatomy, have been exposed and might render this stage of the operation technically difficult.

4. These dissections disclosed that in half of the subjects studied the inferior pancreaticoduodenal arises high up on the superior mesenteric artery and is distributed in a fan-shaped manner downward and outward over the anterior surface of the gland.

5. The gastroduodenal artery is remarkably constant in its origin, course, and distribution, but in 2 of the subjects studied it gave origin to the middle colic artery. It is, therefore, recommended that the origin and distribution of this vessel be determined before the gastroduodenal artery or the inferior pancreaticoduodenal artery are ligated.

6. In many cases traction laterally on the head of the pancreas is necessary in order to dislodge the uncinate process from its position beneath the superior mesenteric vessels. This maneuver may induce a reflex resulting in profound shock because of the large number of sympathetic nerves radiating to the pancreas from the mesenteric plexus. Therefore it is suggested that, as soon as the head of the pancreas is exposed, the plexus be infiltrated with novocain, in the hope that this complication, which we found extremely difficult to combat successfully, may be avoided.

7. The suggestion is made that the placing of a gastroenterostomy be the first step in the second stage of the operation.

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AN ASEPTIC RESECTION OF THE STOMACH FOR CARCINOMA AND ULCER

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CARCINOMA of the stomach is frequently accompanied in patients of advanced age by anemia, debility, poor nutrition, and impaired resistance to infection. Every effort is made before operation upon such patients to minimize the hazards imposed by these conditions by transfusions, by a high protein, high carbohydrate diet, and by the administration of vitamin concentrates for 7 to 10 days preceding the operation. Occasionally, sulfanilimide and, more recently, sulfathiazole have been administered for 24 hours before the operation and for 48 hours after the operation. Despite these various precautions, which may not all be realized because of pyloric obstruction, the hazards remain great. In one clinic, a mortality of 50 per cent has been recorded following resections. In the past 10 years at the Stanford clinic, the mortality in the resected cases has been 10 per cent. In an effort to reduce this mortality still further, an aseptic resection of the stomach has been developed in the past 28 months, independently of a similar development in Wangensteen's clinic (6). Although primarily intended for application in resection for carcinoma, in which, due to achlorhydria, infection is more imminent, we are now employing it also in resection for ulcer. In resection for ulcer, it is freely conceded that in the majority of cases the contamination encountered by entering the lumen of the stomach, the duodenum, or the jejunum does not usually impose a serious risk of infection. However, since one or two patients in every hundred cases of resection of the stomach suffer infected wounds, and occasionally peritonitis and death, an aseptic technique should diminish or prevent such catastrophes. By such improvements and by constant vigilance and endeavor does the surgeon reduce "the irreducible minimum."

From the Stanford University Medical School.
Presented before the Pacific Coast Surgical Association February 20, 1941.

The accompanying illustrations show the various steps in technique.

In all upper abdominal surgery, the optimum position of the patient on the table is obtained by elevation of the upper half of the body, permitting the stomach and liver to descend below the costal margin, and the small intestines to fall into the pelvis out of the operative wound (Fig. 1a). This prevents exposure and handling of the small bowel, both important factors in postoperative distention. In this position, also, pulmonary

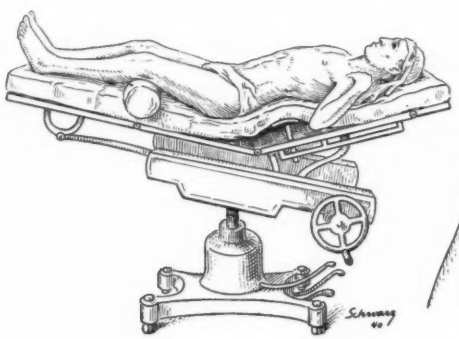

Fig. 1a.

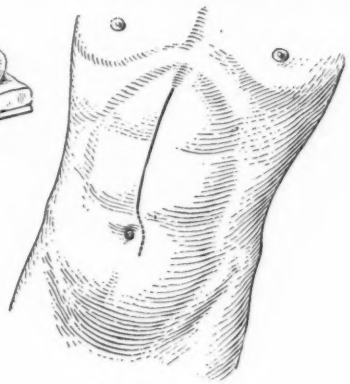

Fig. 1b.

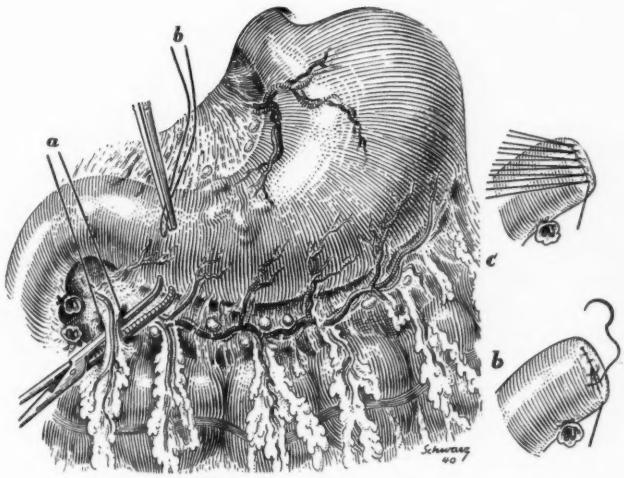

Fig. 2a.

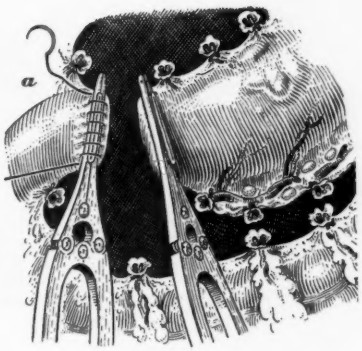

Fig. 2b.

ventilation and respiratory exchange is improved through a more efficiently working diaphragm. A kidney elevator maintains the normal lordosis and elevates the intra-abdominal contents into the wound. By flexion at the hips, the lower half of the body is elevated above cardiac level to prevent pooling of blood in the lower extremities incident to the general vasodilatation that accompanies a general anesthetic.

A midline incision (Fig. 1b) provides easy accessibility both to duodenum and to the cardia of the stomach. On occasion the left costal cartilages close to the sternum are divided without entering the chest, and the ligamentous attachment of the left lobe of the liver is divided to expose the esophageal gastric junction. The incision may be prolonged on either side of the umbilicus as circumstances dictate.

In mobilizing the omentum or the gastrohepatic mesentery, the tissues containing the blood vessels are not crushed by the application of clamps (Fig. 2a). Instead, the tissues are separated by blunt dissection in an avascular area, two ligatures are applied and tied, and the tissue cut between them. Where the tissue cannot be separated easily as in the gastrohepatic mesentery, the two ligatures are applied by transfixion needles introduced through an avascular area, and the vessel is divided between them. The purpose of avoiding clamps is to minimize the crushing and devitalization of tissues in the operative area—thus (1) reducing the postoperative febrile reaction, (2) eliminating as far as possible the need of the body to absorb dead tissue, and (3) minimizing still further the hazard of infection through possible bacterial contamination of avascular tissue capable of acting as an excellent culture medium. It is believed that if the cells in the avascular tissue beyond the ligature are not crushed, their nutrition may be maintained by becoming adherent to surrounding structures or by imbibition of nutrition from peritoneal fluid until revascularization is effected.

The stomach is mobilized, the lesser curvature almost completely, the greater curvature well up to and sometimes including the gastrosplenic ligament (Fig. 2b). Two Payr clamps are applied distal to the pylorus and the duodenum is transected between them with a cautery. The distal duodenal stump is seared by applying the cautery along the Payr clamp for approximately 15 seconds to insure coagulation of the vessels in the divided duodenal wall. A continuous Parker-Kerr basting stitch of No. 0 chromic catgut on an atraumatic needle is applied to the duodenum with the Payr clamp still in place (Fig. 2b, *a*), thus insuring the turning in of the raw edges on

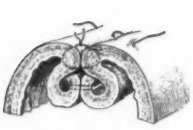

Fig. 3a.

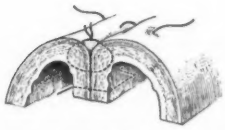

Fig. 3b.

removal of the clamp. This first line of closure is in turn buried by reversing the direction of the same catgut suture back to its site of origin (Fig. 2b, *b*). A third line of *interrupted* black silk sutures is applied (Fig. 2b, *c*), thus burying the two previously placed continuous catgut closures.

In line with previous observations (5) continuous nonabsorbable sutures are never used in gastrointestinal anastomoses. Reichert and Holman found in cleared specimens of intestinal anastomoses of 3 to 6 weeks' duration that the interrupted nonabsorbable silk sutures had migrated so that they lay either underneath the peritoneum, or had been discharged into the lumen and lost. The determining factor seemed to be whether or not the suture had passed into the infected mucosa. If the needle was made purposely to penetrate the lumen, the stitch was discharged into the lumen. If the needle was applied to pass through the submucosa without entering the lumen, the stitch would eventually lie free on the serosal surface covered only by peritoneum. Therefore, a continuous nonabsorbable

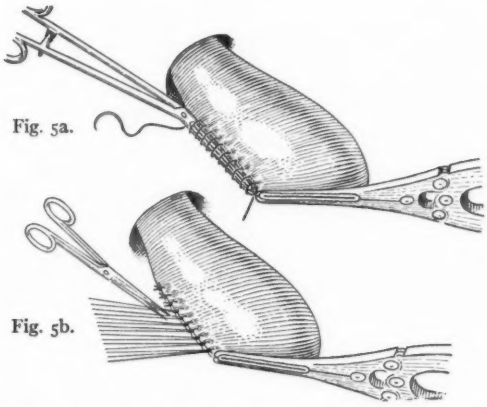

Fig. 5a.

Fig. 5b.

stitch might lie partly underneath the peritoneum, and partly inside the lumen, thus providing a continuous "seton" from sterile peritoneum to the infected lumen. Hence, the necessity of avoiding the use of *continuous* nonabsorbable sutures in intestinal anastomoses.

The Parker-Kerr *inversion* stitch is a fundamental procedure in surgery. It turns into the intestinal lumen the raw, contaminated edge of the divided bowel wall and approximates serosa to serosa (Fig. 3b). As early as 1823, Bichat enunciated this elemental fact, to be applied by Lembert in 1826 to intestinal suturing. Despite the insistence of these early authors that mucosa-to-mucosa will not heal, that serosa-to-serosa is a *sine-qua-non* in intes-

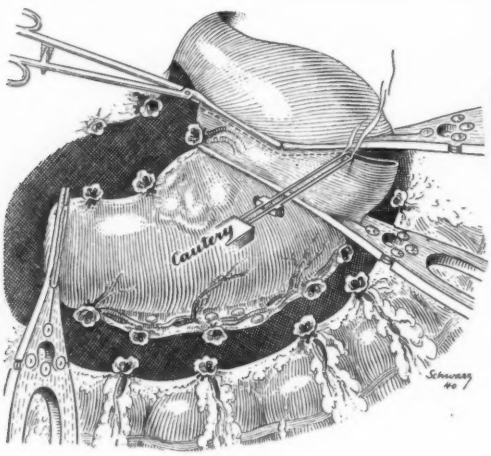

Fig. 4a.

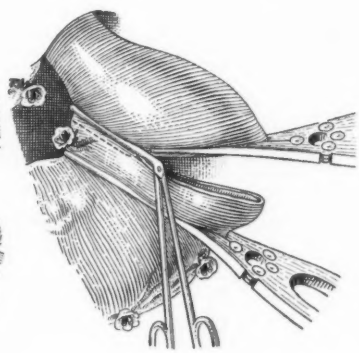

Fig. 4b.

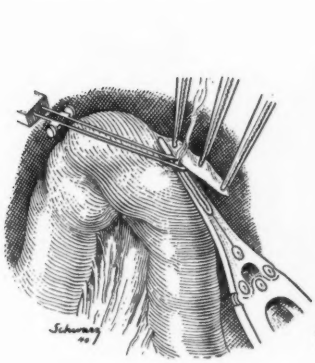

Fig. 6a.

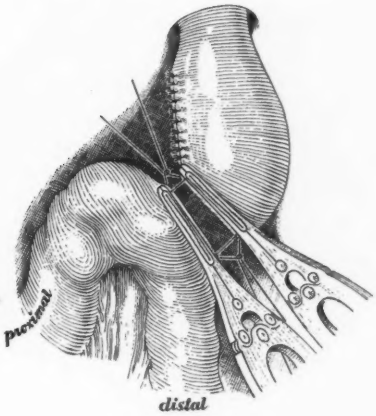

Fig. 6b.

tinal suture, some surgeons are still fond of using either the mattress *eversion* stitch for approximation of surfaces and control of bleeding, or the de Petz clamp, which everts the unsterile bowel edges and applies constricting metal staples to control bleeding (Fig. 3a). The raw edges approximated by this mucosa-to-mucosa stitch are then buried by a serosa-to-serosa suture, thus fulfilling the law of intestinal suturing. However, the buried raw edges of the bowel, infected and avascular, theoretically may invite the formation of small abscesses which may burst into the lumen or the peritoneal cavity, and may cause failure in the line of suture with the formation either of an external fistula or a peritonitis. Granting that this may occur only rarely, its very possibility should be eliminated by avoiding the *eversion* stitch in intestinal suturing.

Payr or narrow crushing clamps are applied to the stomach in one of two ways (Fig. 4a and b), as illustrated, depending upon the ease of application. The stomach is divided with a cautery, and the cut edges of the stomach wall are seared by passing the hot cautery back and forth over the surface of the clamp for 15 seconds. Recently, following the observations of Gerbode in the Stanford Surgical Laboratory, instead of the stomach being divided flush with the crushing clamp, a small cuff of the wall is left projecting 1 to 2 millimeters beyond the clamp. This cuff is seared, thus coagulating and closing the open ends of blood vessels without damaging the gastric wall on the proximal side of the clamp, which may occur if the clamp is excessively heated. Gerbode's observations indicate that the portion of the bowel wall devitalized by the crushing clamp and by the cauterization separates and drops off into the lumen within 48 hours. The resulting raw surface between the opposed intestinal walls which is usually very narrow is covered with mucosa within 18 to 21 days.

The remnant of stomach is partially closed along the lesser curvature, first by a continuous Parker-Kerr basting stitch of chromic catgut on an atraumatic needle (Fig. 5a), thus inverting the raw seared surfaces of the divided stomach wall. The continuous suture is in turn buried by interrupted silk sutures (Fig. 5b). A Payr or narrow-bladed Martzloff or Wangensteen clamp is applied tangentially on the jejunal wall as illustrated in Figure 6a and a segment is removed by cautery, the edges of the bowel being seared again for about 15 seconds to control bleeding. Careful inspection of the removed segment should reveal a mucosal surface along its entire extent.

The loop of jejunum is applied to the stomach remnant (Fig. 6b), proximal arm to right of opening, distal arm to greater curvature.

The two Payr or Wangensteen narrow-bladed clamps on the remnant of stomach and on the jejunum are approximated anterior to the colon (Fig. 7). The anastomosis is effected by one of two ways: A row of interrupted

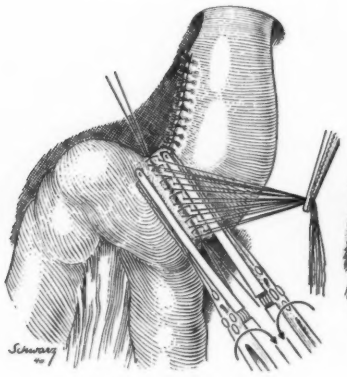

Fig. 7a.

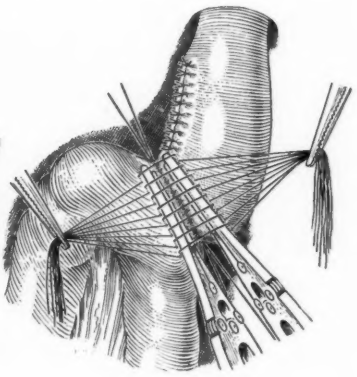

Fig. 7b.

mattress sutures of silk is applied posteriorly, the needle and suture paralleling the clamps as close as subsequent tying will permit. After all have been applied, they are tied.

A row of interrupted mattress silk sutures are applied anteriorly, the needle and suture again paralleling the clamps (Fig. 7b). The clamps are removed and the stitches tied separately. A few additional sutures are applied at the two extremities of the stoma to insure a leak-proof closure. After the last stitch has been tied, the new gastrojejunal stoma is opened by gentle digital manipulation.

This method of approximation of serosal surfaces for re-establishing intestinal continuity (Fig. 7), as used in our early aseptic resections, has been superseded in later resections by utilizing Martzloff's modification of the Parker-Kerr basting stitch as suggested by Wangensteen. The clamps are rotated away from the proposed posterior line of closure. A continuous basting stitch of No. 0 chromic catgut on an atraumatic needle is applied alternately to the contiguous gastric and jejunal serosal surfaces lying posterior to the clamps (Fig. 8a).

The clamps are rotated toward the posterior suture and a second continuous Parker-Kerr basting stitch of No. 0 chromic catgut is applied alternately to the contiguous gastric and jejunal surfaces lying anterior to the clamps (Fig. 8b). The clamps are removed, the two sutures pulled taut, thus accurately approximating the serosal surfaces posteriorly and

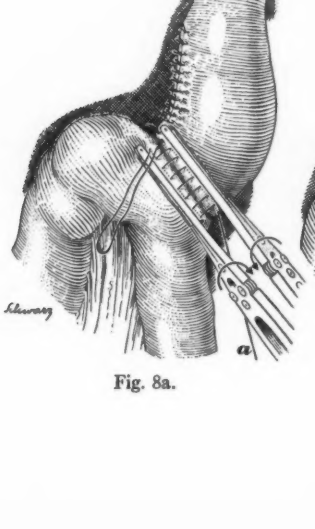

Fig. 8a.

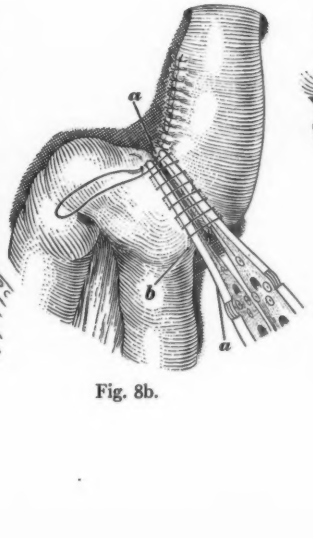

Fig. 8b.

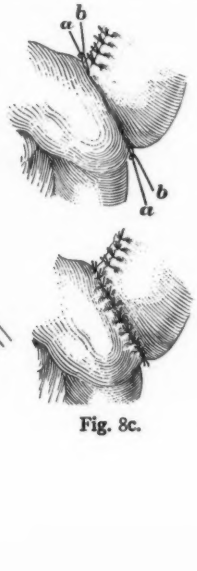

Fig. 8c.

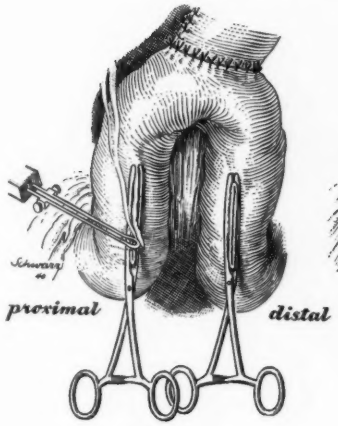

Fig. 9a.

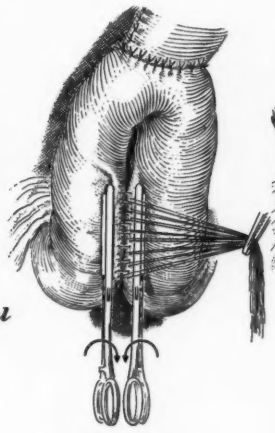

Fig. 9b.

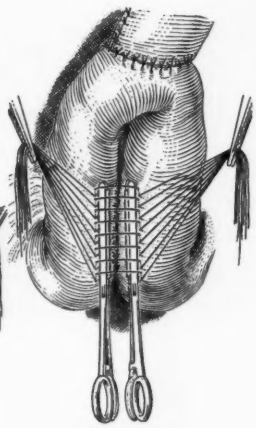

Fig. 9c.

anteriorly. The two sutures are tied together at each end (Fig. 8c, *a*, *b*). This line of continuous catgut suture is in turn buried by interrupted silk sutures applied posteriorly and anteriorly. Digital manipulation insures the opening of the stoma.

In resections for ulcer in which a larger remnant of stomach remains than in resection for carcinoma, this completes the operation.

The larger remnant of stomach following resection for ulcer does not recede into the left upper quadrant, and therefore obstructing angulation of either of the two jejunal arms of the gastrojejunal anastomosis is not so imminent. The *anterior* gastrojejunostomy also contributes to diminishing the danger of such obstructing angulation. Moreover, in resections for ulcer, a jejunojejunostomy between these two jejunal arms of the gastrojejunostomy is strictly avoided, as it is considered highly undesirable to deflect the alkaline duodenal and pancreatic secretions through an enteroenterostomy, away from the gastroenterostomy. The neutralization, preferably in the stomach, of the acid gastric secretions by the alkaline duodenal secretions is most effective in preventing jejunal ulceration.

In all cases of subtotal resections for cancer, in contrast to resection for ulcer, the anterior gastrojejunostomy with a complementary jejunojejunostomy is considered practically obligatory (Figs. 9 and 10). It is our aim in resections for cancer to remove the entire lesser curvature together with the gland bearing tissues in the gastrohepatic mesentery and most of the greater curvature. The small remnant of stomach resulting from this procedure recedes high into the left upper quadrant, under the left diaphragm. Were a posterior gastrojejunostomy performed through a rent in the mesocolon, a drag on the mesocolon would occur, and obstructing angulation of one or both arms of the jejunum would be imminent. Even if this immediate danger were averted, the hazard of a jejunal ulcer or of a gastrojejunocolic fistula is greatly increased by tension on the anastomosis from a fixed or short mesocolon. I propose as an axiom in gastric surgery that following any gastric anastomosis, the stomach must be *comfortable*, both at rest and in activity. Any interference with the effective motility of the stomach, either by the fixed or short mesocolon or by the stomach being joined to the fixed portion of the jejunum, will surely lead to tragic consequences. In resections for cancer, therefore, an anterior gastrojejunostomy is invariably performed and since there is no danger of jejunal ulceration incident to the deflection of the alkaline duodenal secretions away from the gastrojejunal anastomosis, an enteroenterostomy is also performed between the two arms of the jejunum leading to and from the gastric stoma. Two thin-bladed Martzloff or Wangensteen crushing clamps are applied tangentially on the jejunal wall (Fig. 9a), a segment

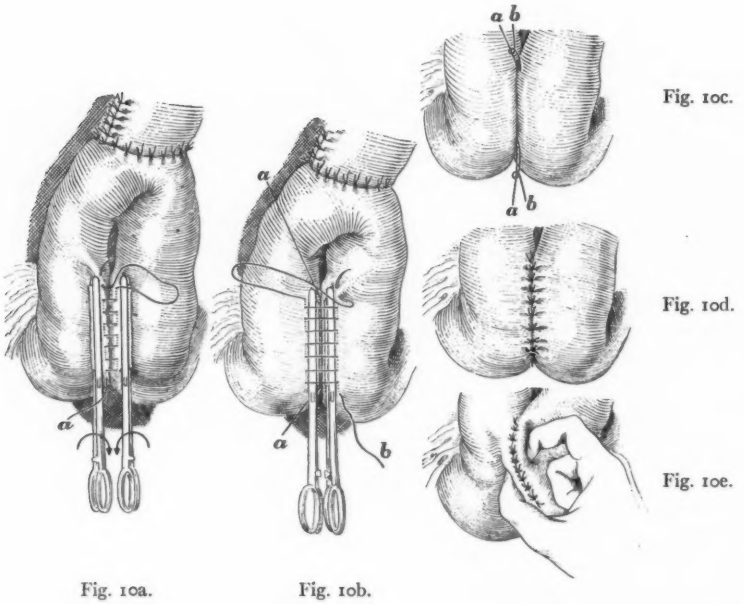

Fig. 10c.

Fig. 10d.

Fig. 10e.

Fig. 10a. Fig. 10b.

of bowel wall is removed by the cautery, the edges are seared for control of bleeding, and an anastomosis is effected by one of two methods: (1) by interrupted mattress silk sutures applied posteriorly and anteriorly parallel to the clamps (Fig. 9b and c), or (2) by the Martzloff application of the Parker-Kerr basting stitch (Fig. 10d and e). The latter procedure is now considered preferable. A continuous No. 0 chromic catgut suture is applied paralleling the clamps posteriorly, the suture passing alternately from one jejunal wall to the contiguous surface of the other (Fig. 10a). The posterior suture remains loose while the clamps are rotated and a similar continuous suture of No. 0 chromic catgut is applied, paralleling the clamps anteriorly (Fig. 10b). The two clamps are removed, and both sutures are pulled taut, thus approximating the apposed serosal surfaces and inverting the raw edges of the jejunum into the lumen (Fig. 10c, *a-b*). These two catgut sutures are tied at both ends without puckering and without reducing the size of the anastomotic opening. The entire anastomosis is reinforced with interrupted silk sutures (Fig. 10d). Digital manipulation insures opening of the stoma (Fig. 10e).

Any available omentum is brought up to lie between the under surface of the incision in the abdominal wall and the underlying viscera. The wound is closed in layers.

In numerous experimental anastomoses and in 31 clinical resections of the stomach for cancer and ulcer, no hemorrhage has occurred or deaths, either from leakage or peritonitis. In not a single patient have we had an infection of the wound or evidence of a localized peritonitis.

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HUMAN BITES OF THE HAND

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EXPERIENCE in many communities has yielded abundant proof of the danger which attends neglect of wounds contaminated with human mouth organisms. As the concomitant sequelae and resultant functional disturbances are often of a most serious nature, the importance of the correct management of the early and late human bite lesions cannot be overemphasized. There is a definite tendency for these infections, when once established, to extend and to invade into deeper and more vital structures, the lesions rapidly becoming foul smelling, necrotizing, and resistant.

The organisms implanted in the tissues of the hand are often most virulent. The part played by such anaerobes as the fusiform bacillus and the spirochete of Vincent has been repeatedly pointed out. Although these organisms are not always demonstrable in cultures and smears from human bite wounds, dark field examination of fresh wet smears will demonstrate their presence in a higher percentage of instances. Anaerobic cultures observed over a period of 7 to 10 days will often yield much information. Streptococci and staphylococci alone and in symbiosis, as well as other contaminants such as the colon bacillus, various fungi, and occasionally the Spirocheta pallida play an important rôle in producing and prolonging these necrotizing infections.

In order to gain a lucid concept of the problems involved in the prophylaxis and treatment of these lesions one must appreciate the anatomic complexity of the tissues which predisposes to extension of infection rather than to localization, particularly under conditions of neglect, as well as the low resistance of fibrous connective tissue and cartilage, to infection.

A knowledge of the mechanism of production, the usual sites of injury, the extent and depth of the lesion, and the possible course of extension of the infection is of considerable aid in the intelligent management of these cases.

Human bite injuries usually occur during the course of fist fights or drunken biting brawls. Consequently, the lesions range from actual bites of the phalanges and hand to puncture wounds and lacerations produced by a fist striking exposed teeth. When the closed fist is used in striking a blow the knuckles of the second and third metacarpals receive the major force of the impact. This is primarily due to the fact that these bones are longer and stronger than the other metacarpals and, furthermore, they are more immobile. In this position the dorsal ligaments, extensor tendons, and skin are tightly stretched across the joint, and a blow on the projecting head of the metacarpal will easily cause a sharp, resisting surface to penetrate the joint cavity or to damage underlying structures (Fig. 1).

A more rare mechanism, that of the sucking of hangnails or of clean lacerated wounds by the patient or a concerned bystander, will account for contamination with mouth organisms in a small number of cases. One of the patients included in our group of late infected cases acquired a severe infection following the biting of a hangnail.

In reviewing our early human bite wounds we have encountered almost twice as many lacerations of the fingers as of the knuckles In the late cases the converse is true. The wounds of the phalanges occur predominantly on the dorsum, the palmar surface only occasionally being involved.

In regard to the extent and depth of the lesions, the injury may present itself as: (1) a simple abrasion over the phalanges, knuckles, or palmar surface of the hand or wrist, involving only the epidermis (Fig. 2); (2) a complete avulsion of segments of skin, subcutaneous structures and occasionally of bone (Fig. 3); (3) a penetrating laceration either partially or completely severing the extensor tendon (Fig.

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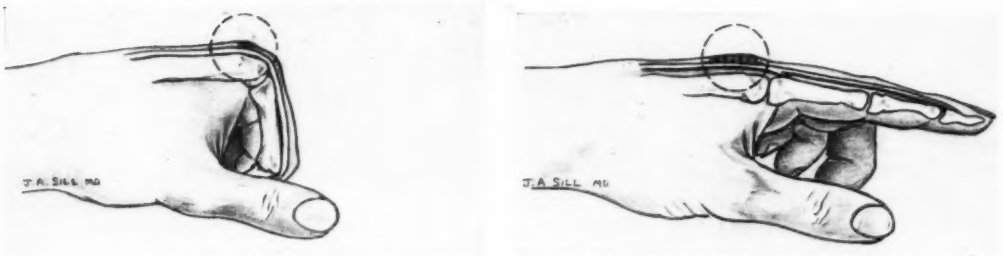

Fig. 1. Region of knuckle. Mechanism of injury and implantation of infection.

4); (4) a wound which may have opened into the dorsal subcutaneous space, subtendinous bursa, dorsal subaponeurotic space, or the joint cavity (Fig. 5).

In 1930, Mason and Koch published a paper on human bite infections of the hand in which they demonstrated experimentally the lines of spread of infectious agents from the region of the metacarpophalangeal joint. This paper has been unsurpassed in the presentation of essentials and remains the outstanding contribution on this subject.

Obviously, abrasions and avulsion lacerations offer little opportunity for the establishment of an anaerobic infection. Lacerations, however, which have penetrated the subcutaneous layers and opened into the subtendinous tissues and joints, present ideal conditions for the production of fetid, necrotizing infections because of the relatively anaerobic conditions, the low resistance of fibrous tissue and synovial membranes, the anatomic complexity of structures favoring the spread of infection, and the presence of traumatized

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 2. Abrasion injury.
Fig. 3. Complete avulsion of finger tip.

Fig. 4. Penetrating laceration. Partial severance of extensor tendon.

tissue. Consequently, the infections occurring on the dorsal aspect of the hand in and about the metacarpophalangeal joint potentially and actually carry the graver prognosis. Because of the shift of tissues particularly about the knuckles, infection may be carried from an original point of entrance to a relatively distant area (Fig. 1).

Infection occurring from an injury over the proximal phalanx may extend both superficial and deep to the expansion of the extensor tendon (Fig. 6a). From this position it may extend along the lumbrical and interosseous tendons to involve the lumbrical space.

Laceration of the extensor tendon with the implantation of infection but without penetration into the joint may occur. Here the extension of infection will be extracapsular and subtendinous, the subtendinous bursa and subaponeurotic space becoming contaminated (Fig. 6a). Should the joint be infected, infection may penetrate into the subtendinous bursa and subaponeurotic space as well as under the expansion of the extensor tendon over the proximal phalanx (Fig. 6b) from which point infection will travel, as described, namely, to the lumbrical canal and large fascial spaces in the palm of the hand (Fig. 7).

The dorsal subcutaneous space is usually involved early. This follows subcutaneous penetration with or without laceration or displacement of the tendon or extension into the joint.

The flexor tendons and their synovial sheaths are rarely invaded from behind. A dense fibrous sheath and the accessory volar ligament serve as an adequate barrier. Late in the course of infection, especially in neglected cases, the flexor tendon sheaths may be invaded.

Believing the results obtained by those surgeons using chemical and electrocautery

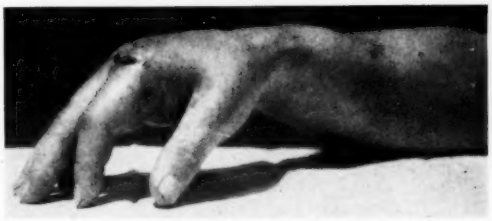

Fig. 5. Penetration of the joint cavity.

methods in the primary treatment of early human contaminated wounds are not entirely satisfactory (1, 2, 3, 5, 8), we have followed in our clinic the suggestion made by Mason and Koch in 1930 of cleansing the wound with soap and water combined with gentle débridement. The recognition of early human bites as such is often quite difficult. Falsification of history is common especially in the white patient, and often results in contraindicated primary suture. A definite and comprehensive regimen has been developed, comprising a searching history, complete examination, and treatment.

The routine treatment employed is as follows: The area about the wound is gently washed with soap and water for 5 minutes following which the wound itself is thoroughly washed with soap and water and irrigated with saline for a further period of 10 minutes. Following this procedure, the edges are gently retracted and the lesion examined, in order to determine the extent of injury if possible. These wounds are not probed since the information obtained is meager and the danger of carrying infectious agents more deeply into the tissues is great. Following mechanical cleansing and a very limited débridement, wet dressings are applied. No attempts are made to repair the rent in the joint capsule. Hands are splinted in the position of function. Lacerations are never sutured nor are injuries to

Fig. 6. a, left, Extracapsular infection. b, Intracapsular infection and extension.

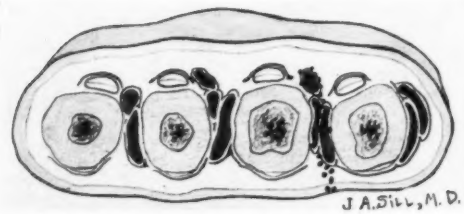

Fig. 7. Lumbrical space and palmar extension.

deeper structures repaired. The major catastrophes in our series have occurred in those cases in which wounds were primarily sutured. Patients return daily for examination and if there is joint involvement, are usually hospitalized. In certain of the initial cases in this series patients were observed and treated in conjunction with Dr. R. E. Speirs who has reported these previously. A total number of 61 early human bites of the hand have been given prophylactic treatment during the past 3 years. All patients seen within 4 hours after the occurrence of injury were considered early cases. Friedrich has pointed out that a lag phase of 6 hours exists before organisms contaminating a wound become acclimated to the human tissues. This lag phase in the case of organisms transferred from the human mouth is greatly shortened and there may be only a brief interval before the organisms are accustomed to their new environment. Those cases already presenting swelling and evidence of infectious extension were not included in this series of early cases even if patients were seen within the 4 hour period and were considered as late cases.

The accompanying table illustrates an interesting grouping of these injuries (Table I). It will be noted that 34 lesions involved the fingers while 18 occurred in the region of the knuckle. Of the total number of cases, 5 showed mild inflammatory reaction characterized by swelling and tenderness without suppuration and only 1 gave evidence of gross infection. Two of the knuckle injuries exhibiting inflammation had been sutured primarily due to falsification of history but the sutures were removed almost immediately and the wound treated as a human bite. One of the compound fractures with the tip of the terminal phalanx completely bitten off showed

TABLE I.—EARLY HUMAN BITES OF THE HAND (TREATED BY SOAP AND WATER WASHING, LIMITED DÉBRIDEMENT, SALINE IRRIGATION, WET DRESSINGS)

Location of injury	No. of cases	Remained clean	Mild inflammation	Gross infection
Compound fracture of finger	6	5	1	0
Finger	34	32	2	0
Knuckle	18	15	2	1
Palm	1	1	0	0
Dorsum	2	2	0	0
Total	61*	55	5	1

*One additional case with extensive multiple injuries of the fifth finger and dorsum of the hand became grossly infected.

mild inflammation (Fig. 3). The compound fractures were usually hospitalized for a short period. The case referred to in the footnote was a most extensive injury, the fifth finger having been almost completely bitten off at the base of the proximal phalanx, tooth injuries of the third and fourth metacarpophalangeal joints and 3 lacerations over the dorsum of the hand. It was necessary to remove the fifth finger. The third and fourth metacarpophalangeal joints became stiff and the dorsal skin sloughed requiring a subsequent graft. Obviously, gross suppuration occurred in this hand, but we were able to save the major portion of the hand and to obtain a fair functional result. In none of the early cases, except the last mentioned, was it necessary to resort to amputation.

A more complete analysis has been made of the last 27 cases. In this group 10 were knuckle injuries, 5 of these occurring on the third right knuckle and 1 on the third left knuckle. Two occurred on the second right knuckle. Of the 17 finger injuries, the first, second, and fifth right fingers were most commonly involved. There were 10 extensor tendon lacerations and 1 flexor tendon laceration. The metacarpophalangeal joint was known to be entered in 3 instances, but no doubt lacerations involving the joint were more frequent than this, as the positive determination of the extent of the injury in this region is often difficult to ascertain.

Over 60 per cent of the cases were between the ages of 15 and 25 years, 18 being males,

Fig. 8. Usual type of incision for adequate joint drainage.

9 females; 19 were colored, and 8 white. Of 22 cases the functional result in 20 was excellent, good in 1, and poor in 1 (cases described previously).

The average wound healing time for the whole series of 61 cases was 8.5 days and for the group of 27 cases 9.9 days.

The after-care consisted essentially of splinting and the application of continuous saline, boric acid, or magnesium sulphate soaks for a period of 48 hours. The wet dressings were discontinued at this time if the wounds remained clean. Splinting was continued to complete healing.

This relatively simple course of management of early human bite injuries has given results which have been most gratifying. Unfortunately, the patient, when first seen often has a fully established infection, and regardless of the adequacy of treatment, frequently is condemned to a prolonged illness which may result in loss of parts and occasionally in loss of life.

Fig. 9. Healed incision. Drainage subcutaneous, subaponeurotic, and joint spaces.

In marked contrast to the prophylactic treatment and management of the early human bite injuries, is the therapeutic problem presented by the late infected human bites. These wounds are already in serious conditions, and sometimes extensively infected. As in other infections of this type, adequate surgery is essential with emphasis on somewhat earlier and more radical drainage. In general, the basic principles enunciated by Kanavel, Koch, Mason, and others relative to the treatment of established hand infections should be adhered to scrupulously. It should be unnecessary and is obviously impractical to outline the treatment in the most minute detail. Suffice it to say, that under general anesthesia, and in a bloodless field, the hand is thoroughly cleansed with soap and water. Then an extremely careful, meticulous débridement is performed, with removal of as much infected, gangrenous sloughing tissue as possible, and in addition with adequate drainage for all areas of infection. Definite mention should be made regarding metacarpophalangeal joint infections. The joint capsule should be opened transversely by a 1 to a 1.5 centimeter incision which usually gives sufficient drainage (Fig. 8). As has been pointed out earlier in the

Fig. 10. Function obtained following drainage of infection of subcutaneous subaponeurotic and joint spaces.

paper, infections of this type when implanted in certain regions may characteristically spread along certain lines to involve adjacent or deeper structures. The deepest anatomic plane involved should be inspected, as the infection may spread along the lowermost plane (Fig. 9). Infection of the joint, if adequately drained, does not always result in a completely ankylosed joint as in many instances excellent function is obtained (Fig. 10). An understanding of the pathogenesis of the advance of infection is essential to the correct surgical management of these severe infections, since it is only by locating those areas of greatest potential danger and recognizing the presence of infection that the lesion can be intelligently and satisfactorily managed. One should be slow to amputate extensively infected fingers but extensive drainage of the soft parts is essential. Often a useful part may be preserved or if amputation later becomes necessary, more of the extremity may be saved. Amputation should be avoided in the presence of an acute infection.

Fig. 11. Drained infection. Dorsal subcutaneous and dorsal subaponeurotic space.

The wounds are then loosely packed with vaseline gauze and usually massive wet dressings are applied. A considerable variety of antiseptic solutions have been employed. In addition to saline, boric acid, and magnesium

Fig. 12. Incision for drainage of lumbrical space.

sulphate solutions, we have utilized and rather favor the use of Dakin's solution; it being our impression that the wounds remained cleaner and that sloughs separated more readily with consequently better drainage when the latter solution was used. Hydrogen peroxide, potassium permanganate, and chromic acid solutions also were used without notable success. Zinc peroxide, arsenicals, and sulfanilamide did not produce strikingly favorable results. The fingers, hand, and arm are then splinted and put at rest in the position of function and whenever possible arranged so that the position will favor dependent drainage. It is our belief that practically without exception cases of this type should be hospitalized. A Wassermann should be done in all patients presenting human contaminated lesions.

As has been stated, the initial injuries in the late infected cases occurring in the region of the knuckle outnumbered those of the fingers. In 34 of the 54 patients the knuckles were involved, 15 occurring over the third metacarpophalangeal joint, the others scattered and of this group of 34 cases, the joint cavity itself was infected in 19 instances. There were 19 cases with lesions of the fingers, 16 injuries being on the dorsal surface, and 3 on the volar surface. In 6 cases the middle interphalangeal joint was infected and in 4 cases the distal interphalangeal joint was involved. As might be expected, partial or complete laceration of extensor tendons occurred in 18 cases and in only 6 cases were the flexor tendons partially severed. There was 1 case presenting a laceration of dorsum of the hand alone.

In several cases there was multiple involvement of joints, fascial spaces, and tendon sheaths. However, in 12 cases infection was confined to the dorsal subcutaneous space and

Fig. 13. Severely infected finger. Amputation required.

in 21 cases both the dorsal subcutaneous and dorsal subaponeurotic space was infected (Fig. 11). Infection of the midpalmar space was present in 3 cases and this seems significant in that this space is not commonly involved in the usual hand infection. In 1 case infection extended from an involvement of the index flexor tendon and its sheath to the thenar space. In another case the ulnar, radial bursa, retroflexor space, and bones of the wrist and hand became so severely infected from a knuckle lesion that amputation through the forearm was required. From an original focus at the metacarpophalangeal joint, infection spread to the lumbrical spaces in 9 cases. Thirteen cases of the total 48 developed stiff fingers and in 5 cases amputation of parts was required, in 1 of which it was necessary to perform amputation through the forearm (Fig. 13).

In spite of the severity of these infections, the average length of healing was 34 days and 9.4 was the average number of hospital days. No fatalities occurred in this group of cases.

As has been noted in the literature (6), these infections are prone to recurrence and frequent exacerbations. In our series there were 3 such instances, 1 in 3 weeks, 1 in 2 months, and 1 in 3 years' time.

Since instituting the described management of early human bite lesions, the number of late cases admitted to the hospital have been definitely fewer in number. For a short interval during a change in the resident staff, the late infected cases increased, and it was found that the treatment of the early cases was not being carried out as outlined.

The careful evaluation of results in the treatment of human bite infections is difficult because of the variations in the virulence of the contaminating organisms and the resistance of tissues. The criterion of the length of stay in the hospital is not a good index of the extent or severity of the infection. These studies have convinced us that good results in the treatment of human bite infections of the hands can be obtained only by attention to details and adherence to surgical principles. Careful cleansing and gentle handling of tissues have reduced our incidence of severe infections and adequate drainage, fixation of parts and irrigation are fundamental necessities in the treatment of the late infections.

SUMMARY

1. The prophylactic treatment of early "human bite" injuries handled under the regimen of soap and water cleansing, limited débridement, wet dressings, and splinting is simple and effective, the results obtained being superior or equal to those attained when actual or chemical cauterization was utilized.

2. The correct management of the "early human bite" cases has reduced the number of late infected cases and we feel that prompt and intelligent treatment of the infected cases has definitely reduced the morbidity and number of disabling and deforming sequelae.

3. In dealing with the late infected cases a clear understanding of the mechanism, depth of penetration, and degree of injury in relation to the spread of established infection is essential for adequate and correct surgical treatment.

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INTERSCAPULOTHORACIC AMPUTATION FOR MALIGNANT TUMORS OF THE UPPER EXTREMITY

A Report of Thirty-one Consecutive Cases

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INTERSCAPULOTHORACIC amputation is an operation devised to remove the entire upper extremity, the shoulder girdle, and its muscular attachments. The operation has been variously designated as "removal of one-half of the shoulder girdle" by von Eiselsberg, "surgical removal of the breast girdle" by Adelmann and "extirpation of the arm and shoulder" by Kocher, but it is the term "interscapulothoracic amputation" which the French surgeons, notably Berger, have employed and which now enjoys popular usage.

In the *Anatomy of the Human Body* by W. Cheselden, there is a note and illustration concerning the case of Samuel Wood, a miller, who in 1737 survived a traumatic amputation of an arm and shoulder, caused by an entwined rope attached to the cogs of a mill wheel. Only slight shock was said to have followed this amputation by avulsion. The English surgeon, R. Cumming, has been generally accredited with having performed the first elective operation of this type which was for a gunshot wound, although Halstead maintained that Larrey was the originator of the formal procedure, as it is done today. Dixie Crosby, in 1836, was the first American surgeon to perform a successful extirpation of the shoulder girdle for tumor. In 1837, Musey of Cincinnati did a scapulectomy following a disarticulation of the humerus for sarcoma; the patient survived 30 years.

Until 1881, i.e., before the area of antisepsis, there were 29 recorded interscapulothoracic amputations for various indications, with an operative mortality of 38 per cent. The technique of the operation was standardized by Berger, and the classical procedure still bears his eponym; in 1887 he described all the previously published cases and added his own experience with the operation, for which his mortality rate was 10.4 per cent. The most important article dealing with this subject in medical literature was written by Buchanan of Pittsburgh, who analyzed all the reported cases prior to the year 1900. At that time the operation was so unusual as to be a surgical curiosity and surgeons were inclined to rush their individual case reports into press before final end-results could be appreciated. Buchanan, by letter and consultation, secured most of the follow-up data on 141 interscapulothoracic amputations which were done prior to the year 1900.

Our analysis of the evolution of this operation, the indications, and contraindications for it, the modifications of techniques employed, and the final end-results achieved will therefore be presented in three parts: (a) A summary of the Buchanan report, which is a thorough analysis of 141 operations done prior to 1900 (Table II). (b) An analysis of 180 additional case reports from the medical literature from 1900 to date (Table III). This would indicate that the operation is done with surprising infrequency. A complete bibliography of 357 references originally appended to this article revealed the fact that the operation is universally done. These references to articles which appeared in Russian, Japanese, Swedish, Dutch, Portuguese, Italian, Spanish, Hungarian, Roumanian, and Polish medical literature have necessarily been deleted from this article because of insufficient space. Russian surgeons as a national group have probably applied this radical procedure more often than others and, moreover, have contributed

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TABLE I.—COMPARATIVE END-RESULTS OF SCAPULECTOMY AND INTERSCAPULOTHORACIC AMPUTATION—KAWAMURA (1909)

	Total No.	Survivals		Operative deaths	
		No.	Per cent	No.	Per cent
1. Incomplete scapulectomy	28	24	85.7	4	14.3
2. Complete scapulectomy	66	59	89.4	7	10.6
	94	83	88.3	11	11.7
3. Interscapulothoracic amputation	227	208	91.6	19	8.4

some interesting modifications of the operation (Tikhor, Sapezhko, Ilchenko). (c) A report of 31 personal cases from the bone and mixed tumors services of the Memorial Hospital (Table IV). These 31 unselected, consecutive interscapulothoracic amputations were all done for malignant tumors of the upper extremity and were performed without an operative death.

INDICATIONS FOR INTERSCAPULOTHORACIC AMPUTATION

The necessity for performing such a massive, disabling, and disfiguring amputation demands a clear conception of the indications, hazards, natural history of the tumor responsible, and possible end-results to be achieved. The idea of sacrificing the clavicle, scapula, and arm with their muscular attachments is so repugnant to most patients and repellent to many surgeons, that one of three sequences is apt to follow. The patient refuses with finality all operative aid, or accepts a more conservative though less certain treatment, or eventually agrees after a prolonged interval, during which the disease advances to the stage wherein an operation of desperation is substituted for what was originally an operation of hope. It may be said in all fairness to the operation, which is unquestionably well conceived, that too few of them are done as carefully planned, elective, initial procedures and too many are performed as a last resort following one or more recurrences after incomplete or more conservative operations. The indetermination or reluctance of the patient is not a contraindication from the sur-

TABLE II.—BUCHANAN'S ANALYSIS OF END-RESULTS, PRIOR TO 1900

Sex	Cases
Male	93
Female	39
Not given	9
Total	141
Age by decades	
0 to 10	8
11 to 20	27
21 to 30	22
31 to 40	24
41 to 50	24
51 to 60	12
61 to 70	4
71 to 80	2

Pathological diagnoses[1]	Cases		Cases
Sarcoma unclassified	105	Carcinoma	7
Malignant tumor unclassified	8	Encephaloma	2
Osteosarcoma	1	Medullary growth	1
Chondrosarcoma	3	Colloid growth	1
Myxosarcoma	4	Chondroma	7
Lymphosarcoma	1	Benign tumor	1

Location of tumor	Cases		Cases
Humerus and upper arm	55	Soft parts—shoulder	11
Scapula	24	Axilla	4
Clavicle joint	1	Carcinoma of shoulder	2
Shoulder joint	1	Recurrent cancer of breast	4
Humerus and scapula	15	Location not stated	12
Clavicle and scapula	3	Secondary involvement of shoulder joint	12
Clavicle and humerus	3		
Clavicle, scapula and humerus	6		

Operative deaths—11.3 per cent	16

Cause	Cases	Location of tumor	Cases
Shock	7	Upper arm	3
Hemorrhage	2	Scapula (alone)	5
Infection	1	Shoulder	3
Other causes	6	Breast	1
		Location not stated	4

	Total	Dead	Living With disease	Living Without disease
End-results				
Total	89	44	11	34
0 to 6 mos.	27	17	6	4
7 to 12 mos.	20	11	3	6
13 to 24 mos.	18	10	2	6
2 to 3 yrs.	3	3	..	..
3 to 4 yrs.	3	..	..	3
4 to 5 yrs.	1	..	..	1
5 to 10 yrs.	12	3	..	9
11 to 20 yrs.	4	..	..	4
21 to 30 yrs.	1	..	..	1

Cause of death	
Operative deaths	16
Local recurrences	7
Pulmonary metastasis	28
Not stated	9

[1]Some of these operable cartilaginous tumors were immense. G. C. Hall of Allahabad removed one weighing 33 pounds and Shepherd of Montreal removed one which was 30 inches in circumference.

TABLE III.—SUMMARY OF REPORTED CASES IN MEDICAL LITERATURE—1900 TO DATE

	Cases
Sex	
Male	123
Female	50
Sex not stated	7
Total	180

Youngest 2½ yrs.; oldest 72 yrs; average, 30½ years

Age by decades	Cases		Cases
0–10	6	41–50	29
11–20	37	51–60	31
21–30	20	61–70	11
31–40	33	71–80	2

Pathological diagnoses	Cases		Cases
Osteogenic sarcoma	41	Spindle cell sarcoma	14
Chondrosarcoma	11	Neurosarcoma	7
Chondroma	8	Schwannoma	1
Myeloid sarcoma—bone	5	Rhabdomyosarcoma	1
Giant cell "sarcoma"—bone	7	Angiosarcoma	1
Lymphosarcoma—bone	1	Perithelioma	2
Endothelial myeloma	1	Sarcoma unclassified	38
Round cell sarcoma	15	Melanoma	1
Lymphosarcoma	1	Squamous cell cancer	6
Mixed cell sarcoma	6	Adenocarcinoma of breast and axilla	6
Myxosarcoma	1	Malignant tumor unclassified	3
		Diagnosis not stated	4

Location of tumor	Cases		Cases
Humerus and upper arm	95	Soft parts—shoulder	7
Scapula	24	Axilla	9
Clavicle	2	Carcinoma of arm and shoulder	5
Scapula and clavicle	6	Recurrent cancer of breast	4
Scapula and humerus	9	Location not stated	1
Clavicle and humerus	3	Secondary involvement of shoulder joint	22
Clavicle, scapula and upper arm	7		
Shoulder joint	8		

Previous operations[1]	Cases
Radical mastectomy	5
Resection of humerus	2
Shoulder joint disarticulation	5
Amputation of arm	2
Excision—cancer in burn scar	2
Formal incisional biopsy	5
Local excision of tumor	30

Method of interscapulothoracic amputation	Cases
Typical Berger technique	115
Le Conte modification (Elliot, Harrington, Vaughan, Jeanbrau)	11
Kocher anterior approach (Powers, Lund, Brin, Murphy, Pomonorov)	7
Littlewood posterior approach (Sondermayer, Parakh)	2
Conjoined radical mastectomy (Cushing, Fischer)	2
Kuster method (Knierim, Troitzky)	2
Method not stated	41

TABLE III.—Continued

	No.	Per cent
End-results—180 cases (collected)		
Operative deaths	9	5
Lost to follow-up	78	43.3
Dead		
From local recurrence	12	6.7
From pulmonary metastasis	31	17.3
From intercurrent diseases	7	3.9
Total	50	27.7
Living[2]		
With recurrence	5	2.8
Without disease	38	21.2
Total	43	23.9

Of the 34 patients with malignant tumors, living and well and remaining under observation, the average post-operative survival period was 16.2 months. The distribution of survival periods was as follows:

0–6 mos	16
7–12 mos	3
1–2 yrs	5
2–3 yrs	8
3–4 yrs	0
Over 4 yrs	2

[1]Fifty-one of the 180 patients had undergone other operations prior to the interscapulothoracic amputation. Of these, 35 patients had 1 operation, 7 had 2, 4 had 3, 3 had 4, 1 had 5, and 1 had 6 previous operations. The types of previous operations are listed.

[2]Of the living patients, 4 had benign tumors (chondromas) and were known to be living and well for 6 months, 7 years, 12 years, and 27 years, respectively, following the interscapulothoracic amputation.

geon's viewpoint. The ultimate psychological effect of this operation on our patients has not been bad; those who are living are apparently happily adjusted to this handicap.

The indications for this operation may be enumerated in the following decalogue:

1. Non-neoplastic conditions, such as extensive trauma with irreparable damage; gunshot wounds, tuberculosis, incurable osteomyelitis. It is not the purpose of this critique to discuss these indications at length.

2. Intractable pain caused by incurable tumors of the shoulder girdle even though metastases to lungs are present. The purpose here is palliation only, in getting rid of a cumbersome, painful, often suppurating extremity (Polosson, Jeanbrau). This indication is not so valid now that intolerable pain in the shoulder and arm can often be controlled by such neurosurgical measures as cervical chordotomy and posterior rhizotomy.

3. All malignant tumors requiring disarticulation of the humerus at the shoulder. The more major procedure in our experience does not require the penalty of a higher operative

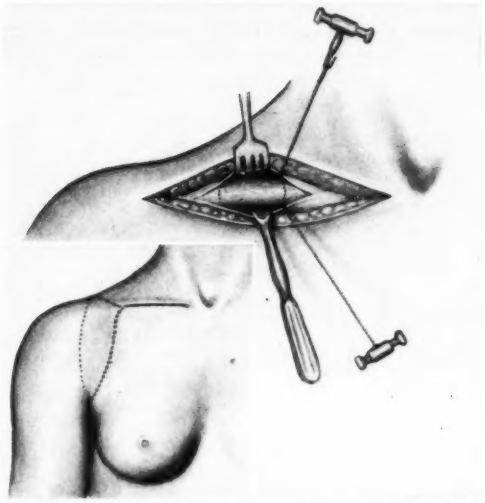

Fig. 1. Incision for preliminary division of clavicle for ligation of axillary vessels and exposure of brachial plexus. Insert shows skin incision.

mortality. The deformity is greater but suitable prosthetic appliances are available and any good tailor can reconstruct the shoulder of a coat. The shoulder without the arm is practically useless. There can be no argument about the greater freedom from local recurrence which interscapulothoracic amputation affords.

4. Many bone sarcomas proximal to the elbow. Periosteal sarcomas, sclerosing osteo-

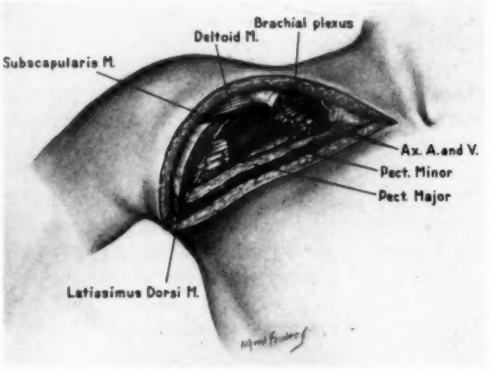

Fig. 3. Division of nerves and vessels, pectoral muscles, and latissimus dorsi muscles.

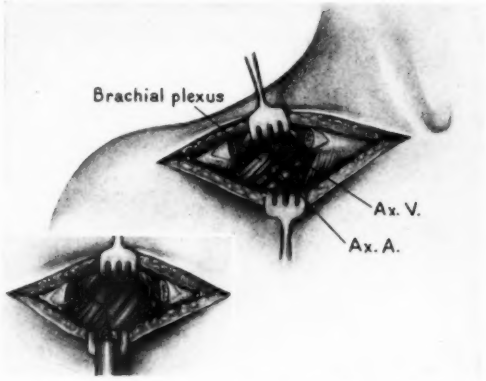

Fig. 2. Double ligatures placed on axillary artery and vein and single ligature on nerves. Insert shows injection of nerves above ligature with 95 per cent alcohol.

sarcomas and others of low grade malignancy; those well confined to the bone, and those involving the lower half of the humerus may be treated by more conservative amputations at the discretion and experience of the operator. But the majority of the other bone sarcomas, particularly those involving the upper end of the humerus; those extending upward through the entire medullary cavity and those which have extended beyond the confines of the bone to infiltrate surrounding normal tissues, are more suitable for interscapulothoracic amputation.

5. The rule of Halstead and Corner that the amputation should be performed above the proximal attachments of the muscles which pass over it. Although this is a good fundamental principle, it is perhaps too radical to be all-inclusive, because some neurosarcomas and osteosarcomas of low grade malignancy may be treated more conservatively.

6. All malignant tumors invading the shoulder joint capsule.

7. Infiltrating malignant tumors involving the deltoid, subscapularis, and pectoral muscles. This rule applies invariably to the unencapsulated neurosarcomas, rhabomyosarcomas, and fibrosarcomas but exceptions are admitted in the case of liposarcomas and the occasional lymphosarcomas which extend beyond the lymph nodes to involve the surrounding soft tissues. In the case of these

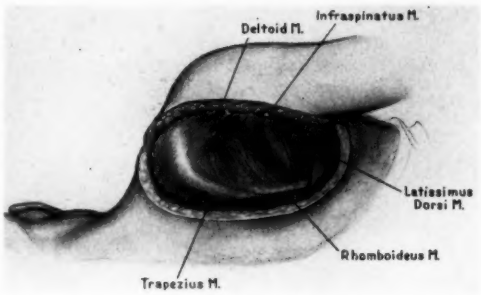

Fig. 4. The incision carried posteriorly shows the muscles attached to the scapula.

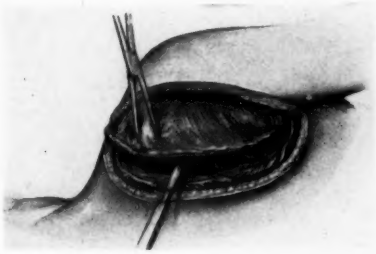

Fig. 5. Volsellum grasping scapula near the vertebral border. Scalpel dividing muscles along the vertebral border and beneath it (subscapularis muscle).

latter two tumors, preliminary radiation therapy or even irradiation alone is the first procedure of choice. Encapsulated neurosarcomas, liposarcomas, or rhabdomyosarcomas may be successfully treated in some instances by radical dissection of the muscle groups containing these tumors with preservation of the extremity

8. Inoperable axillary tumors adherent to blood vessels, brachial plexus, shoulder joint and muscles, permitting no attempts at local excision, however radical.

9. Sarcomas of the clavicle or scapula. Interscapulothoracic amputation is indicated (for these tumors) only when the location of these sarcomas is so intimate to the shoulder joint that partial or complete scapulectomy or resection of the clavicle would not be possible or feasible, and especially if the arm is useless and painful. The entire scapula may safely be removed without too great disability and

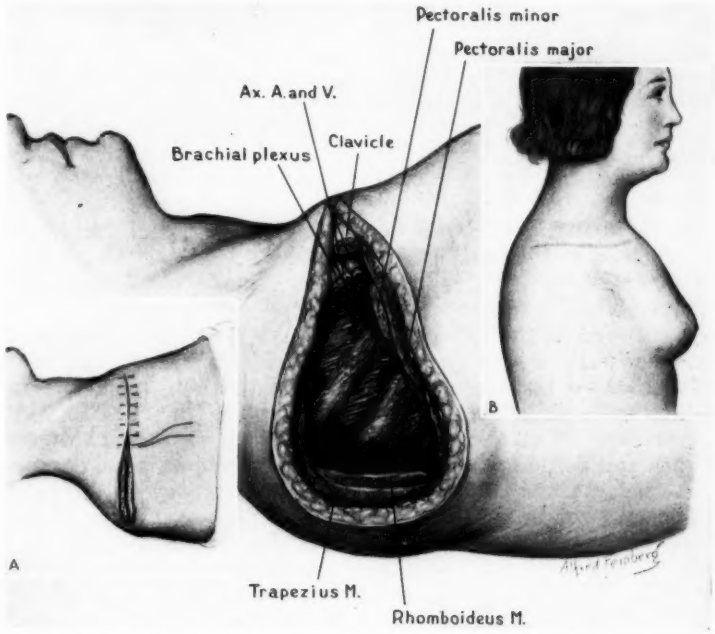

Fig. 6. Wound ready for closure. Inserts demonstrate transverse linear scar.

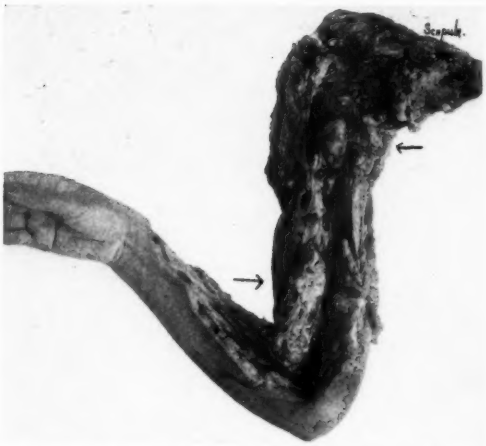

Fig. 7. Case 7. Malignant melanoma, primary on the hand with metastases to epitrochlear and axillary lymph nodes and diffuse linear extension by permeation through the arm. Gross specimen shows extent of involvement. The mass in the upper arm was almost microscopically indistinguishable from neurosarcoma.

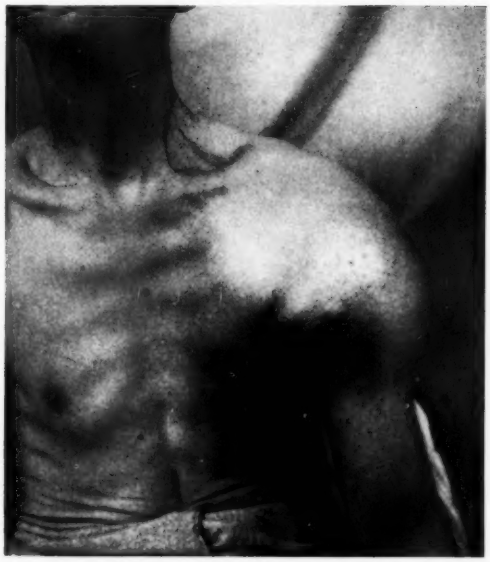

Fig. 8. Clinical photograph of type and regional location of tumor suitable for interscapulothoracic amputation. Osteosarcoma developing on basis of Paget's disease of bone, Case 10 (see Table IV).

with preservation of the arm, if involved by chondrosarcoma or osteosarcoma of low grade malignancy.

10. Relatively benign tumors causing symptoms and disability because of their size and location, e.g., certain huge chondromas developing in the neighborhood of the shoulder joint.

OPERATIVE TECHNIQUE

A. The Classical Berger Operation

The patient is placed on his back with the involved shoulder elevated so that the skin can be prepared by antisepsis well beyond the midline, front, and back. The corresponding arm is well wrapped from fingers to shoulder and left free and mobile to be held by an assistant. By this means the arm may be held in various positions to facilitate the anterior or posterior dissection of the shoulder. Tourniquets and Wyeth pins are unnecessary.

A linear incision is first made over the middle third of the clavicle and this incision is extended through the soft tissues to the periosteum. The middle third of the clavicle is now resected, usually with a Gigli saw. Through this window the subclavian vessels are exposed, with the artery more deeply situated beneath the vein. At this point the modification of LeConte may well be given, as he advocates the resection of the entire clavicle, beginning with the sternoclavicular joint, for the avowed reason that this procedure does afford a better exposure of the subclavian vessels, particularly the artery which is to be ligated first, and it enables the operator to recognize and ligate the suprascapular and transverse cervical vessels. This complete claviculectomy does give better exposure and is absolutely indicated if the clavicle is involved by the tumor, but it must be admitted that there are greater dangers of air embolism and injuries to the pleural dome and thoracic duct (on the left side).

After exposure of the neurovascular bundle at the base of the neck, the subclavian artery is divided between ligatures of heavy black silk, and the vein is treated in a similar manner. The proximal stump of the artery and vein are always doubly ligated. The original skin incision is then carried almost to the tip of the acromion after which it is extended downward along the anterior axillary border.

Fig. 9. Case 15. Operative specimen of amputated hand and forearm. Note congenital neurogenic contractures of fingers associated with localized neurofibromatosis of this extremity. Multiple neurosarcomas appeared, first of hand, later of forearm (see cut), later of upper arm and finally of shoulder, necessitating interscapulothoracic amputation.

The arm is then drawn across the body and the posterior flap is outlined by an incision of the skin along the vertebral border of the scapula, which unites with the anterior incision along the lateral axillary border. The arm is then swung back to its original position and the anterior incision is deepened as far as the pectoral muscles. Division of the pectoral muscles now gives an excellent exposure of the brachial plexus. The surface of the plexus is painted with 10 per cent cocaine and/or 2 per cent novocain solution is injected into the nerve trunks. After division of the various

Fig. 10. Case 15. To illustrate the anatomical defect and character of the scar. This patient is now living and well more than 6 years following this operation for neurogenic sarcoma.

nerve components of the plexus, the ligated proximal stumps are injected with small quantities of 95 per cent alcohol to lessen the possibility of amputation neuromas and causalgia. The arm is now brought forward again and the muscles of the posterior flap, along the vertebral margin of the scapula, are divided. Care is taken to clamp, sever, and ligate the transverse cervical artery before it retracts, if this has not been done at an earlier stage. With the scapula freed of its muscular attachments, the amputation is complete. The bleeding vessels are ligated with fine silk. The skin can usually be closed with interrupted black silk sutures. It heals with a surprisingly good linear scar. Since the adoption of the silk technique there has been less need for the use of drains. Skin grafting is resorted to in instances in which the size and the location of the tumor and the degree of skin involvement require a greater sacrifice of skin.

The patient is usually able to be out of bed on the third postoperative day and home

Fig. 11, left. Case 16. Roentgenogram of osteosarcoma developing in a fractured bone cyst with persistent non-union.

Fig. 12. Case 16. Osteogenic sarcoma. Clinical photograph illustrating regional location of tumor necessitating interscapulothoracic amputation.

within 2 weeks. One of our patients had such good primary wound healing that she was able to start a 600 mile automobile trip on the ninth day after operation.

B. The Anterior or Pectoral Approach of Kocher

The only difficulty encountered during the Berger operation is the exposure of the subclavian vessels. The anterior approach suggested by Kocher avoids this handicap and in our hands has proved to be a welcome modification of the original operation. After the middle third of the clavicle has been resected, the ligation of the subclavian vessels is postponed until the anterior incision is carried through the pectoral muscles into the axilla. This part of the dissection is similar to the same phase in a radical mastectomy as the axillary artery and vein come immediately into view. With the more adequate exposure afforded by enlargement of the operating field, the subclavian vessels are more readily located and the underlying artery mobilized and ligated without the previous hazard of injuring the overlying vein.

From this point on, the operative technique is exactly similar to that described.

C. The Posterior or Retroscapular Approach of Littlewood

According to some advocates, particularly Knaggs, the posterior approach of Littlewood may be done with greater speed and more anatomical exactness. After division of the midthird of the clavicle, the posterior flap is outlined first and then the scapula is freed from its medial and superior muscular attachments. The supposed advantage of this technique is that when the neurovascular bundle is encountered from the posterior aspect, the subclavian artery appears first, the vein second, and the brachial plexus last, in the exact order desired for ligation and severance.

D. Additional Operative Details

Cairo (1924) suggested a 2 stage operation in old patients, first disarticulating the hu-

Fig. 13. Case 19. Left, Ulcerating, fungating neurogenic sarcoma of forearm, treated by amputation through upper arm. Recurrence later developed in the axilla, which was then treated by interscapulothoracic amputation.

Fig. 14. Case 19. Character of wound 18 days after interscapulothoracic amputation.

merus and then doing the scapulectomy later.

LaFaye did not resect the clavicle, but ligated the axillary vessels and disarticulated the humerus and the scapula from the clavicle.

Kuster added a vertical excision over the sternomastoid muscle to the handle of the racquet incision along the clavicle. He asserted that this gave a better exposure of the subclavian vessels and that it was particularly helpful in permitting primary ligation of the transverse cervical artery and vein.

COMPLICATIONS

Interscapulothoracic amputation is a radical, major, and dramatic operation, but it is really a simple and safe procedure once the subclavian vessels are securely ligated. The exposure of these vessels is occasionally very difficult due to the location of certain bulky tumors which overlie the operative field. In thin-chested individuals, especially when the arm has long been useless, the subclavian vessels as they lie on the first rib must be looked for considerably above the clavicular incision. With the danger of hemorrhage avoided, the patient subjected to this operation is relatively safe. In one of our recent patients, the subclavian vein was accidentally opened during a difficult attempt to free the artery; air was audibly aspirated into the vein, hemorrhage although great was controlled by compressing the vein with a finger against the first rib, and the patient went into shock. He was restored by immediate transfusion as the vein was repaired and the operator allowed to proceed with the amputation. The patient recovered from this experience without any late complications. One of von Bergmann's patients died from hemorrhage caused by extension of the cancer around the subclavian vessels; this surgeon made a heroic effort to save his patient by tying off the superior vena cava.

Shock is minimal when proper preoperative and sustaining measures are in use, such as blood transfusions, usually given concurrently during the operation using the opposite arm or leg. Due to fixation of the tumor, the pleural cavity may be entered with the complications characteristic of pneumothorax. Injury to the thoracic duct by a left interscapulothoracic amputation may conceivably occur, but we have never seen or read of this occurrence.

CONSERVATIVE OPERATIONS VERSUS INTERSCAPULOTHORACIC AMPUTATION FOR MALIGNANT TUMORS

In the previous listing of indications for interscapulothoracic amputation, the comparative values of this radical procedure with more conservative operations have been considered. The practicability of the irradiation of certain liposarcomas and lymphosarcomas and the dissection of muscle groups containing encapsulated rhabdomyosarcomas and neuro-

sarcomas of low grade malignancy is recognized. One of us (B. L. C.) has published a series of case reports of scapulectomy for malignant tumors; the osteochrondrosarcomas of this bone may attain a large size without metastasizing. Although this operation has proved successful in the hands of some surgeons, the cases should be properly selected. In an unbiased study of 65 malignant tumors of the scapula, Nancrède reported that not one patient had been cured by conservative measures.

In selecting one of these more conservative procedures, such as scapulectomy or disarticulation of the humerus, the surgeon should do so with the firm belief that it is wholly sufficient as far as the local tumor is concerned, and not because he relies on another opportunity for local cure through a secondary or subsequent interscapulothoracic amputation. (Table I.)

The Tikhor-Linberg operation. An operation planned by the Russian surgeon Tikhor and applied afterward by Bauman and Linberg has for its purpose the excision of the scapula, clavicle, and head of the humerus with preservation of an extremity which functions slightly. A racquet incision is made along the clavicle, and the pectoral muscles are divided. The brachial nerve plexus and the subclavian artery and vein are dissected free and spared. A circular incision around the humerus determines the lower level of the resection and the humerus is sawed through. By a posterior incision over the scapula, this bone together with the clavicle and upper segment of the humerus is sawed through. By a posterior incision over the scapula, this bone together with the clavicle and upper segment of the humerus is resected. The biceps and triceps muscles are sutured to the intercostal muscles anteriorly and posteriorly. At the completion of the operation the lower arm, forearm, and hand are intact, and the functions of the forearm and hand are partly retained, but of course shoulder and upper arm movements are no longer possible. A study of the case reports of this operation lends support to the belief that it is palliative only, because the patients who have not died have required subsequent operations for recurrences.

ADVANTAGES OF INTERSCAPULOTHORACIC AMPUTATION OVER DISARTICULATION FOR MALIGNANT TUMORS OF THE UPPER ARM

The following advantages of interscapulothoracic amputation over disarticulation for malignant tumors of the upper arm may be mentioned:

1. The lymphatics and veins are removed at a much higher level.

2. The shoulder muscles with their natural fascial planes are entirely removed, which is especially important if the tumor has shown invasive tendencies.

3. The more radical operation not only permits dissection of the axilla but a removal of the axillary boundaries.

4. The mortality is no greater. The 31 consecutive interscapulothoracic amputations reported in this article were done without an operative death which is proof enough of the safety of this operation.

5. The wounds resultant after interscapulothoracic amputation heal more satisfactorily as there are practically no dead spaces to be obliterated.

6. The deformity is greater but not enough to be a deciding factor.

7. Interscapulothoracic amputation is often done for a malignant tumor recurrent in the stump of the disarticulation. This very fact would indicate that the original disarticulation had not been wisely chosen as the proper operation. Consecutive operations finally terminating in interscapulothoracic amputation appear in every reported series, including our own (see Cases 15, 19, and 29 in Table IV). A patient with a neurosarcoma or fascial sarcoma of the hand, wrist, or forearm relates a history of one or more local excisions with recurrences developing each time proximal to the scar; finally amputation of the forearm, later of the arm, and still later disarticulation of the humerus may be done for proximally recurring tumors usually with increasing degrees of malignancy. Yet in retrospect for each individual patient in whom this series of events occurs, few surgeons would advise so radical a primary procedure as interscapulothoracic amputation for a sarcoma originating, for example, in the forearm.

END-RESULTS

In a comparative study of end-results grouped in periods of medical effort, the statistician must carefully analyze the collected data for sources of possible error. For example, the number of long term survivals of patients with "sarcoma" following interscapulothoracic amputation listed in Buchanan's report prior to 1900 is much greater than the number surviving in the series we have collected and which were reported from 1900 to date. The surgical technique, facilities for early diagnosis, and more detailed knowledge of the life history of these malignant tumors have unquestionably improved, and yet the same good end-results are not achieved. The explanation probably lies in correct histological classification and diagnosis, for example, giant cell "sarcoma" of bone is now more commonly referred to as benign giant cell tumor of bone.

Histological type of tumor in relation to age of patient. As the sarcomas which comprise the majority of tumors for which this operation is done, are more common in young adulthood, the average age of 33 years for these patients is what would be expected. Because the operation does not cause much surgical shock, it may be safely done in the case of elderly patients, if there are no other contraindications. The youngest patient was 12 years and the oldest patient was 72 years of age.

The average ages of patients with the different histological types of tumors for which this operation was done was: with osteogenic sarcoma, 23 years; with other malignant bone tumors, 48 years; with neurogenic sarcoma, 38 years; with rhabdomyosarcoma, 52 years; with melanoma malignum, 40 years; and with squamous cell carcinoma, 63 years.

Eighteen of the 31 interscapulothoracic amputations were for malignant bone tumors. During the past 6 years, there has been a growing tendency at the Memorial Hospital to perform this operation more frequently for neurosarcomas and rhabdomyosarcomas of the upper arm and shoulder.

Duration of symptoms in relation to histological type of tumor. (*Memorial Hospital Series.*) The malignant tumors of the soft somatic tissues, i.e., neurosarcomas, rhabdomyosarcomas, and soft part sarcomas of undetermined histogenesis, present a longer latent period between the date of the first symptoms and the interscapulothoracic amputation, than do the malignant bone tumors, not because of slower growth or lessened degree of malignancy but because the necessity for a radical surgical procedure does not seem so urgent. Patient and surgeon alike are more content to temporize with conservative measures if the sarcomas do not involve bone. Primary or immediate interscapulothoracic amputation is more likely to be acceptable and to be done for malignant tumors of bone than for sarcomas of the soft somatic tissues. For example, the duration of symptoms before this operation for the various histological types of tumors was: for osteogenic sarcoma, 6 months; for other malignant tumors of bone, 4 months; for neurogenic sarcoma, 60 months; for rhabdomyosarcoma, 16 months; for other soft part sarcomas, 25 months; for squamous cell carcinoma, 36 months; and for malignant melanoma, 3 months.

Type of previous operation (*Memorial Hospital Series*). In our experience, the formal incisional biopsy of sarcomas is a dangerous operation and from the viewpoint of prognosis should almost be considered a major procedure. The so called local excisions of soft part sarcomas, as performed at the Memorial Hospital, are not enucleations but radical dissections with sacrifice of normal tissues surrounding the neoplasm. Thirteen, or 42 per cent, of our 31 patients had undergone previous operations, such as formal incisional biopsy, 5; local excision, 1; 2 excisions, 1; 3 excisions, 1; 5 excisions, 1; 7 excisions 1; and lesser amputations, 2.

Type of operative technique (*Memorial Hospital Series*). Twenty-one of the interscapulothoracic amputations were done according to the Berger classical procedure. The 10 remaining operations were performed chiefly during the past 5 years by the Kocher anterior and pectoral approach which will undoubtedly gain favor because it can be performed with greater ease and safety.

Effect of preoperative irradiation on end-results (*Memorial Hospital Series*). Of the

TABLE IV.—INTERSCAPULOTHORACIC AMPUTATIONS PERFORMED AT THE MEMORIAL HOSPITAL, NEW YORK, 1924–1940

Case Number	Date of operation	Age Sex	Duration of symptoms	Previous operations	Location	Histological type	Type of Operation	Supplementary treatment		Cause of death		Post-operative duration	Comments on progress
								Preoperative	Postoperative	Metastases	Recurrence		
1. L.B.	6–21–24	63 M	3 yrs.		Arm, with extensive axillary and supraclavicular metastases	Squamous carcinoma	Berger pinch grafts	Interstitial irradiation, 200 kv. x-ray therapy			*	9 yrs.	Two dissections for recurrence, 10–17–25 and 4–2–30. No evidence of disease 3–27–32. Death 6–14–33
2. G.P.	12–23–27	53 M	15 mos.	Excision	Scapula, soft tissue	Neurogenic sarcoma	Berger	200 kv. x-ray therapy			Yes	22 mos.	No evidence of disease for 18 months after operation
3. F.C.	12–27–27	36 M	2 mos.	Biopsy	Axilla and neck	Anaplastic, suggests transitional cell carcinoma, possibly metastasis from carcinoma of thymus	Berger	200 kv. x-ray therapy Coley's toxins	Coley's toxins	Lungs		2 mos.	
4. R.W.	7–18–28	14 F	2 mos.		Humerus	Osteogenic sarcoma	Berger		Coley's toxins, radium element pack therapy	Lungs	Yes	2 yrs.	No evidence of disease for 18 months after operation
5. R.B.	9–19–28	13 F	1 mo.		Humerus	Osteogenic sarcoma	Berger	200 kv. x-ray therapy		Lungs		1 yr.	
6. B.S.	9–10–29	17 M	2½ mos.		Humerus	Osteogenic sarcoma	Berger	100 kv. x-ray therapy		Lungs		1 yr.	
7. H.F.	9–18–29	40 F		3 excisions	Hand, arm, axilla	Melanoma	Berger		200 kv. x-ray therapy	Lungs		13 mos.	
8. J.C.	1–29–30	48 M	4 mos.		Humerus	Plasma-cell myeloma	Kocher			Sarcomatosis		21 mos.	No evidence of disease for 16 months after operation
9. D.M.	1–29–30	14 M	1 mo.		Humerus	Osteogenic sarcoma	Berger	200 kv. x-ray therapy Coley's toxins			Yes	10 mos.	
10. J.Z.	2–6–30	57 M	2 mos.		Humerus	Osteogenic sarcoma on Paget's disease	Berger	200 kv. x-ray therapy		Lungs		16 mos.	
11. J.H.	3–4–31	19 M	2 mos.	Biopsy	Humerus	Osteogenic sarcoma	Berger	Coley's toxins		Lungs		5½ mos.	
12. S.K.	6–17–31	33 F	5 mos.		Humerus	Osteogenic sarcoma	Berger		200 kv. x-ray therapy, Radium element pack therapy	Lungs		7½ mos.	
13. J.O'B.	10–16–31	15 F	6 mos.	Aspiration biopsy	Humerus	Osteogenic sarcoma	Berger	Coley's toxins, radium element pack therapy		Lungs		9 mos.	
14. H.G.	11–4–31	35 M	7 mos.		Humerus	Osteogenic sarcoma	Berger	Coley's toxins			Yes	13 mos.	
15. D.D.	2–25–35	24 M	5 yrs.	7, including amputation of the forearm	Upper arm	Neurogenic sarcoma	Berger	200 kv. x-ray therapy	200 kv. x-ray therapy			5 yrs. 8 mos.	Resection for recurrence in brachial plexus, 10 months after operation. Living, with no evidence of disease

TABLE IV.—INTERSCAPULOTHORACIC AMPUTATIONS PERFORMED AT THE MEMORIAL HOSPITAL, NEW YORK, 1924–1940—Continued

TABLE IV.—INTERSCAPULOTHORACIC AMPUTATIONS PERFORMED AT THE MEMORIAL HOSPITAL, NEW YORK, 1924–1940—Continued

Case Number	Date of operation	Age Sex	Duration of symptoms	Previous operations	Location	Histological type	Type of Operation	Supplementary treatment		Cause of death		Post-operative duration	Comments on progress
								Preoperative	Postoperative	Metastases	Recurrence		
16. J.B.	3–25–35	23 M	10 yrs.		Humerus	Medullary spindle cell osteogenic sarcoma	Berger					5 yrs. 7 mos.	Bone cyst with persistent non-union and growth one year prior to admission. Living, with no evidence of disease
17. K.H.	11–20–35	12 F	2 yrs.		Humerus	Osteogenic sarcoma	Berger pinch grafts	Radium element pack, 200 kv. x-ray therapy. Coley's toxins				5 yrs.	Living with no evidence of disease
18. D.C.	7–22–36	15 M	2 mos.		Humerus	Osteogenic sarcoma	Berger	200 kv. x-ray therapy		Lungs		8 mos.	No evidence of disease 4 months after operation
19. W.T.	7–23–36	47 M	12 yrs.	Biopsy and amputation of arm	Massive tumor recurrent in arm and axilla	Neurogenic sarcoma	Kocher		200 kv. x-ray therapy	Lungs Skin	Yes	32 mos.	Home on the 9th postoperative day. No evidence of disease for 3 months. Recurrence at 13 months after operation, treated with 200 kv. x-ray therapy and interstitial irradiation. Posterior rhizotomy for pain
20. D.C.	5–27–37	38 M	14 mos.	Aspiration biopsy	Scapula	Synovioma	Berger		200 kv. x-ray therapy	Lungs Ileum	Yes	3 yrs. 3 mos.	No evidence of disease 2 years after operation. Recurrence excised
21. A.B.	9–24–27	35 F	6 mos.	Aspiration biopsy	Humerus	Osteogenic sarcoma	Kocher	200 kv. x-ray therapy		Lungs		5 mos.	
22. A.C.	9–29–37	72 M	11½ mos.	Amputation through arm	Humerus	Rhabdomyosarcoma	Berger	200 kv. x-ray therapy		Lungs	Yes	11½ mos.	No evidence of disease 7 months after operation. Recurrence
23. F.R.	11–20–37	20 M	10 mos.		Humerus	Osteogenic sarcoma	Berger			Lungs		23 mos.	No evidence of disease 20 months after operation
24. I.H.	2–28–38	58 F	40 mos.	Aspiration biopsy	Upper arm	Rhabdomyosarcoma	Kocher	200 kv. x-ray therapy		Lungs		16 mos.	No evidence of disease 15 months after operation
25. A.C.	3–2–38	34 M	23 mos.	Biopsy	Upper arm	Neurogenic sarcoma	Kocher	200 kv. x-ray therapy				2½ yrs.	Living, with no evidence of disease
26. Y.H.	8–16–38	48 F	2 mos.	Biopsy	Humerus	Rhabdomyosarcoma	Kocher		200 kv. x-ray therapy	Lungs right buttocks		8 mos.	No evidence of disease 4 months after operation. X-ray therapy to metastases in right buttocks
27. E.B.	4–25–39	25 F	14 mos.	Biopsy	Clavicle	Fascial sarcoma	Kocher	Radium element pack therapy		Lungs		8 mos.	No evidence of disease 3 months after operation. Pregnancy complicated the case
28. H.H.	9–27–39	47 M	4 yrs.	2 excisions	Axilla	Paraganglioma	Kocher	200 kv. x-ray therapy Gold radon seeds				1 yr.	Living, with no evidence of disease
29. E.S.	11–8–39	30 M	5 yrs.	5 excisions	Upper arm	Neurogenic sarcoma Grade III	Kocher					11 mos.	Living, with no evidence of disease
30 V.S.	2–2–40	17 M	6 mos.		Humerus	Osteogenic sarcoma	Berger			Lungs		6 mos.	
31. W.G.	5–14–40	28 M	1 yr.	2 excisions	Scapula and axilla	Rhabdomyosarcoma	Kocher pinch grafts	200 kv. x-ray therapy				4 mos.	No evidence of disease one month after operation. Living, with recurrence and pulmonary metastases

*Apoplexy.

Of 31 consecutive interscapulothoracic amputations performed at Memorial Hospital, 17 were done during past 6 years. With 3 exceptions operations were done by the authors on patients from bone and mixed tumor services.

TABLE V.—END-RESULTS OF INTERSCAPULOTHORACIC AMPUTATION (MEMORIAL HOSPITAL SERIES)

End-results	No.	Per cent
Total cases	31	100.0
Dead		
From pulmonary metastasis	15	48.4
From pulmonary metastasis and recurrence	4	12.9
From local recurrence	3	9.7
From sarcomatosis	1	3.2
From apoplexy	1	3.2
Total	24	77.4
Living		
With pulmonary metastasis	1	3.2
Without disease	6	19.4
Total	7	22.6

patients surviving at the time of this report, 2 who had no preoperative irradiation are clinically well for 11 and 67 months, respectively, after the operation. Five patients who had preoperative irradiation are living, 1 with metastasis 4 months later, and 4 without clinical evidence of recurrence for 20, 30, 60 months, respectively. Rocher and Papon assert that preliminary irradiation permits later interscapulothoracic amputation, but no case reports were presented to support this contention. The application of irradiation as a means of avoiding this major amputation is a different matter entirely from the selective use of irradiation as a preoperative measure. It is different to evaluate the benefits of such therapy and it certainly cannot be done by a study of our own end-results, because we have been so liberal in giving x-ray and radium therapy to these patients. One would think that interscapulothoracic amputation would suffice as the sole treatment if the line of incision were well above the upper limits of the tumor and that any preoperative adjuvant measures would be superfluous. Nevertheless, our past experience in dealing with sarcomas of the soft somatic tissues of other regions has indicated that there is greater freedom from local recurrence and distant metastases if preliminary irradiation is given. This is especially true for the liposarcomas. The reason for this is hard to fathom unless it could be that the trauma which is associated with the operation causes immediate dissemination of metastases; the lethal or abiotic action of the preliminary x-ray or radium therapy could conceivably lessen this hazard.

TABLE VI.—POSTOPERATIVE DURATION IN RELATION TO TYPE OF TUMOR (MEMORIAL HOSTAL SERIES)

Histological type of tumor	Number of cases	Postoperative duration in months	Range in months
Osteogenic sarcoma	15	18.5	5 to 67
Neurogenic sarcoma	5	31.0	11 to 60
Soft part sarcoma (undetermined histogenesis)	3	19.7	8 to 39
Malignant bone tumor other than osteogenic sarcoma	1	21.0	
Rhabdomyosarcoma	4	9.9	4 to 16
Squamous cell carcinoma	1	108.0	
Melanoma	1	13.0	
Malignant tumor unclassified	1	2.0	
Total cases	31	21.8	5 to 108

Patients living at the time of report (Table V). Of the osteogenic sarcoma group 2 patients were without disease, 60 and 67 months, respectively; of the neurogenic sarcoma group, 3 were without disease, 11, 30 and 60 months, respectively; of the soft part sarcoma (undetermined histogenesis) group, 1 was without disease, 12 months; and of the rhabdomyosarcoma group, 1 was living with recurrence and pulmonary metastases, 4 months. The patient with squamous cell carcinoma lived 9 years without evidence of recurrence or metastasis and then died of apoplexy.

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TREATMENT OF PERITONITIS

Intraperitoneal Use of the Sulfonamides Based Upon Animal Experiments

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THE bacteriostatic effect of the sulfonamides[1] is a well established fact in the mind of the clinician, and the ever increasing literature serves to signify that this mode of action has a sound experimental basis while the details of its inhibitory effect are still in the theoretical stages.

In a very comprehensive article, Lockwood advances a hypothesis which supplies a theoretical framework upon which a complete scheme of sulfonamide chemotherapy may be constructed. He specifies the following 3 principal factors which should tend to modify the curative effect of the sulfonamide compounds: (1) concentration of the drug maintained in the immediate environment of the bacteria; (2) the mobilization of cellular defenses; (3) concentration of sulfonamide inhibitor substances. It is with the first factor that we find our chief interest in this experiment.

It is reasonable to believe that if the local concentration of the drug can be immediately elevated and maintained at the site of action of the invading organism or at an anatomical or pathological point, the chances for a favorable outcome should be greatly superior to a route of administration which primarily promotes an elevated concentration systemically.

As to the ability to kill beta hemolytic streptococcus *in vitro*, Colebrook, Buttle, and O'Meara have definitely shown no essential difference between sulfanilamide-laden blood from a treated patient and chemically treated blood from a normal individual.

Many workers (3, 7, 9) in various fields have endorsed the drugs as valuable for their local effectiveness. During the past year the attention of many abdominal surgeons has been drawn to the possibilities of intraperitoneal use of the sulfonamides in the treatment of peritonitis. Thompson, Rosenburg, Dees, and others have reported the intraperitoneal use of crystalline sulfanilamide in the treatment of appendiceal peritonitis. It has been our experience from clinical and necropsy findings that powdered material in the peritoneal cavity is quickly walled off by omentum and is ultimately dependent upon absorption and systemic concentration for its local effect.

We have carried out a series of animal experimentations in which we attempted a comparative study of the sulfonamides in solution or suspension by the systemic and local routes of administration.

In order to study this problem, it was necessary to produce an experimental appendiceal peritonitis comparable to that in man. The method described by Bower, Burns and Mengle (1) was used: The mesentery and base of the appendix were ligated and a large dose of castor oil was given to produce perforation and generalized peritonitis.

The wounds were sutured in layers, a small opening being left at the upper end where a through and through mattress suture was left untied. After 12 to 18 hours, the skin was prepared with iodine and alcohol, and a sterile sponge forceps was introduced into the peritoneal cavity and rotated in a stirring motion to insure a generalized spread of the infection, and to a certain extent, simulate the spread and trauma associated with the operation. Sterile applicators were then inserted for cultures, and the mattress sutures were tied. Postmortem cultures were not taken because, usually, the animals had been dead an hour or two before being discovered.

As shown by Bower, Burns, and Mengle (2), the bacteriology is strikingly similar in man and dog and, therefore, results obtained

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[1] "Sulfonamide" is employed to include the three drugs of greatest current use: sulfanilamide, sulfapyridine, sulfathiazole.

in these experiments should be quite similar to those expected in man. The bacteriology of our experiments is summarized in Table I. Plain agar, blood agar, Endo's agar and anaerobic brain-heart infusion broth were routinely inoculated, and transfers to the various sugars were made as necessary to identify the individual organisms. The high incident of Clostridium welchii leads one to the conclusion that had therapeutic serum been used, the mortality rate could have been lowered appreciably. This was the original intention of the authors, but Army reserve commissions interrupted the study (Table I).

There were 5 groups of 10 dogs each, 1 group of 12 dogs, and 1 group of 8 dogs. The results are tabulated in Table II and discussed more fully under individual experiments. The larger number of dogs in the bacteriological table is explained by the fact that many dogs died within 24 hours or that their wounds drained spontaneously and thus were discarded from the reported groups (Table II).

TABLE I.—BACTERIOLOGY OF EXPERIMENTALLY PRODUCED APPENDICEAL PERITONITIS IN 86 CONSECUTIVE DOGS

Organism	Dogs	Percentage
Staphylococcus albus	28	32.5
Anaerobic streptococcus	24	27.9
Bacillus coli	23	26.7
Streptococcus fecalis	3	3.4
Clostridium welchii	13	15.1
Gram positive rod of the listerella group	11	12.8
Nonhemolytic streptococcus	6	6.9
Staphylococcus aureus	6	6.9
Streptococcus viridans	5	5.8
Clostridium tetani	3	3.4
Proteus vulgaris	2	2.3
Staphylococcus citreus	2	2.3
Aerobacter aerogenes	1	1.16
Gram negative rod of Salmonella group	1	1.16
Sarcina lutea	1	1.16
Anaerobic staphylococcus	1	1.16
Hemolytic streptococcus	1	1.16

EXPERIMENT I

A control group of 10 dogs was established with a mortality rate of 100 per cent. This group consisted entirely of adult dogs whose wounds did not drain and who survived more than 24 hours. Dogs dying within 24 hours would not allow time for treatment and were, therefore, unsatisfactory for other experiments.

Dogs in this group were given food and water, as in all groups, but received no treatment. The wounds were opened in 24 hours for culture and then the mattress sutures were tied. These dogs all developed signs and symptoms of generalized peritonitis, characterized by leucocytosis, elevation of temperature, vomiting, and abdominal rigidity and tenderness. The average duration of life was 41.4 hours; most of the dogs died at 36 hours.

The standards agreed upon in the selection of this group were rigidly adhered to in all of the following experiments.

EXPERIMENT II

A group of 10 dogs was used in which treatment was started within 18 hours by an 0.8 per cent solution of sulfanilamide subcutaneously. One daily dose of 0.14 grams per kilogram of body weight was given in small amounts over the neck and back. Care was used not to overdistend the tissues in any one area, but in spite of this, most of the surviving animals developed skin sloughs. The average sulfanilamide blood level was 6.0 milligrams per cent and the highest obtained was 16.0 milligrams per cent. Of the dogs not surviving the experiment, the average duration of life was 55 hours. Autopsy showed no gross evidence of damage to the liver or kidneys but did show cloudy purulent peritoneal fluid and redness of peritoneum. The 5 surviving dogs (50 per cent) killed and subjected to postmortem examination later, showed only a few adhesions to the cecum and lateral wall.

EXPERIMENT III

Sulfanilamide (0.8 per cent solution) was administered intraperitoneally in 2 doses daily totaling 0.07 grams per kilogram of body weight. The dosage was reduced to 0.07 grams per kilogram of body weight because the first group of dogs given a dose of 0.14 grams per kilogram of body weight all expired within a few hours. Autopsy, however, failed to reveal any reason for the rapid death.

The drug was administered through a large bore needle which was found most convenient for these animals. Tubes sutured in place were pulled out by the animals, and drainage tracts resulted.

In this group the mortality rate was 50 per cent with an average survival of 58 hours. The

TABLE II.—COMPARATIVE STUDY OF SULFONAMIDES IN THE TREATMENT OF EXPERIMENTALLY PRODUCED APPENDICEAL PERITONITIS IN DOGS

Experiments	Number of dogs	Number of deaths	Number of recoveries	Mortality per cent
I. Control	10	10	0	100
II. Sulfanilamide subq. 0.14 gm/kg	10	5	5	50
III. Sulfanilamide, intraperitoneally 0.07 gm./kilogram daily divided doses	10	5	5	50
IV. Sulfanilamide, intravenously 0.14 gm./kilogram daily divided doses	10	8	2	80
V. Sod. Sulfapyridine, intraperitoneally 0.07 gm./kilogram daily divided doses	12	6	6	50
VI. Sulfathiazole, intraperitoneally 0.14 gm./kilogram daily	10	4	6	40
VII. Sulfabenamide, intraperitoneally 0.14 gm./kilogram daily	8	7	1	87

highest blood level observed was 12 milligrams per cent, the average being 2.8 milligrams per cent. The peritoneal cavity of the dogs succumbing to the infection contained dark, greenish brown, purulent fluid, sloughed appendices but no leakage from the cecum. The surviving dogs killed 2 weeks after cessation of treatment showed normal peritoneal cavities except for a moderate amount of free fluid which, in 2 cases, was definitely bloody. The liver and kidneys were grossly normal.

EXPERIMENT IV

This group was treated with sulfanilamide (0.8 per cent solution) intravenously, in 2 doses daily, totaling 0.14 grams per kilogram of body weight. The mortality rate was 80 per cent with an average survival of 48.5 hours. The average blood level was 4.0 milligrams per cent.

The autopsy findings in this group were not significantly different from those of Experiment II.

EXPERIMENT V

Sodium sulfapyridine, 1 per cent solution, was given this group of animals intraperitoneally in 2 doses daily, totaling 0.07 grams per kilogram of body weight. The mortality rate was 50 per cent; average survival 46 hours. The blood level in all the dogs, 12 hours after dosing, was below 1 milligram per cent. All dogs not surviving the experiment showed purulent fluid and generalized peritoneal inflammation. One abdomen contained a large amount of bloody fluid. Of the survivals, 2 showed very small omental abscesses (2 to 5 c.cm.), whereas the 3 others had normal peritoneal cavities with very few adhesions. No gross liver or kidney damage was observed in either group.

EXPERIMENT VI

Sulfathiazole, being somewhat less soluble than the other sulfonamides, was given in 1 per cent solution and suspension, and it was so well tolerated that 2 doses daily, totaling 0.14 grams per kilogram of body weight were given. The mortality of this group was 40 per cent; the average survival time, 38 hours. The average sulfathiazole blood level was 4.3 milligrams per cent with 22.9 milligrams per cent the highest observed.

Postmortem examinations on death showed generalized peritonitis and purulent fluid. The appendices were sloughed in all cases yet the ligatures at the cecum held. Of the 6 surviving dogs killed 1 week later, 2 had 300 to 500 cubic centimeters of bloody fluid with an injected peritoneum. The 4 other surviving dogs had very small omental abscesses containing about 5 cubic centimeters of purulent exudate at the ileocecal juncture. Otherwise, the peritoneum was normal.

EXPERIMENT VII

In this group sulfabenamide (4-N-caproamidobenzenesulfonhydroxamide) was dissolved in one-tenth normal sodium hydroxide and neutralized with normal lactic acid. The resultant 1 per cent solution was nonirritating and, according to Moore et al. is caproylaminobenzenesulfinic acid which is thought by other observers to retain some therapeutic activity. Eight dogs were treated in this group by 2 intraperitoneal doses daily, totaling 0.14 grams per kilogram of body weight. Seven, 87 per cent, of the 8 dogs died having 57 hours as an average survival time. The 12 hour blood levels in these dogs were all below 1 milligram per cent. The drug itself was not considered responsible for the deaths, as twice this dosage was given intraperitoneally as a single dose to normal animals with no apparent bad effects.

The necropsy findings of the succumbed animals were those of generalized peritonitis. Autopsy on one surviving dog showed only a few adhesions in the region of the cecum. Although the mortality rate does not speak well of the therapeutic efficacy of this drug, the experiment does eliminate the possibility of any of the animals in other experiments being saved by parenteral fluids rather than from specific action of the drugs administered.

ANALYSIS OF STUDY

The primary intention of this experiment was to determine the therapeutic value of the sulfonamides when applied locally in the treatment of peritonitis. Sulfanilamide was used as a standard to develop a safe and effective route of administration. The results as tabulated in Table II would seem to indicate that subcutaneous or intraperitoneal administration is preferable to the intravenous method. This is best explained by the relatively short action of the drug when given by the intravenous route.

Of the 4 drugs used intraperitoneally, sulfathiazole seems to be the most effective. This may in part be due to the fact that part of the drug was given in suspension which provided a longer time of action before complete absorption took place. We fully realize that the number of dogs in each group is too small for positive and definite conclusions, but we are certain that any one of the sulfonamides may be administered intraperitoneally with safety and without deleterious effect to the peritoneum or intraperitoneal organs. The usual toxic manifestations, of course, must be anticipated and treated appropriately if they arise.

Sulfanilamide intraperitoneally in the treatment of peritonitis seems definitely and unquestionably of value as proved by Mueller and by Jackson. In all of these cases, the drug was given in powder form. This necessitated a large initial dose, and any indicated subsequent intraperitoneal therapy with powder was difficult or was restricted to some other form and route of administration. Sodium sulfapyridine has been used intraperitoneally in a 4 per cent solution in 10 cases at The Oklahoma University Hospitals. The results have been spectacular and the ease of administration remarkable. It can be given through the drainage tube in small divided doses or larger single doses, or by a continuous drip method, and repeated checks on the blood level can dictate the necessary dosage. In none of the cases in which the drug was given only by the intraperitoneal route were serious toxic manifestations encountered. There is evidence to indicate that combined therapy may be more hazardous.

CONCLUSIONS

1. Sulfanilamide, sodium sulfapyridine, or sulfathiazole may be administered intraperitoneally in solution or suspension in proper dosage, with no deleterious effect.
2. Intraperitoneal use of the sulfonamides is effective in the treatment of peritonitis.
3. Of the three sulfonamides, sulfathiazole appears to be the most effective in the local treatment of peritonitis.
4. Subcutaneous administration of sulfanilamide frequently resulted in skin sloughs.
5. Proper dosage is essential. The usual toxic manifestations may be expected and treated appropriately.

The authors wish to acknowledge the splendid cooperation of Ida Lucille Brown Wallace, instructor in the Department of Bacteriology, University of Oklahoma School of Medicine, who made the bacteriological studies in this experiment.

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RETROCECAL APPENDIX

Its Diagnosis and Surgical Approach

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THE single definite diagnostic feature of retrocecal appendicitis is a vertical line of tenderness, starting at the iliac crest, 6 to 8 centimeters behind the anterior superior spine and extending vertically upward, the distance of the involved appendix, often to the rib margin.

The intensity of the initial symptoms is modified by the position. Both pain and vomiting are initially slower in their development and less intense in character. The appendicitis syndrome from the appendix situated retrocecally can be compared to the syndrome of obstructive lesions of the lower bowel. The clinical picture of high bowel obstruction is similar to the freely placed acute appendicitis, while retrocecal appendicitis presents a clinical picture similar to that of lower bowel obstruction. Some systematic differential plan, as suggested by Sloan[1], should be borne in mind in confirming the general diagnosis of appendicitis before the search for localization is begun.

The following method of approach permits the removal of a retrocecal appendix with a minimum amount of contamination of the peritoneal surface.

The incision is made parallel to and about 2 centimeters lateral to the outer rectus margin, starting about 8 centimeters above the level of the umbilicus and following the outer margin of the rectus abdominis down to the level of the internal pillar of the external abdominal ring. This incision is curved with the convexity directed outward. The incision is carried down to the fascia of the external oblique; the fascia is exposed for the entire length of the skin incision (Fig. 1).

At the level of the anterior superior spine of the ilium and about 1 centimeter lateral to the border of the rectus muscle, the external oblique aponeurosis is incised vertically, and this incision is extended upward and downward to the limits of the skin incision (Fig. 2). The fibrous aponeurotic margins of the external oblique separated by the incision are held by hemostats as landmarks in closure (Fig. 2).

The internal oblique and transversalis muscles are separated by blunt penetration with scissors to the preperitoneal fat, then by hooked digital retraction directed upward and downward are separated horizontally in the direction of their fibers, thus exposing the outer surface of the peritoneum and the preperitoneal fat. The under surface of the transversalis muscle is now separated from the peritoneum below to the level of the inguinal ring, above to the upper level of the incision, medially the peritoneum remains in its normal anatomic relation, but laterally and posteriorly from the iliac fossa, from the tip of the iliac crest around the posterior surface of the cecum, reaching medially to the level of the ureter, so that the cecum can be mobilized and the posterior wall can be elevated and rotated anteriorly and medially.

Palpation of the posterior wall of the cecum now discloses the tumor of the inflamed appendix (Fig. 3). Turning the cecum anteromedially, directing the posterior wall anteriorly, and retracting outside the peritoneum (the overlying small bowel), access may now be had to the peritoneum overlying the diseased area (Fig. 3). The peritoneum is intact until this next step.

Fig. 1. Wide separation of external oblique aponeurosis from internal oblique.

Fig. 2. Digital retraction of internal oblique and transversalis from peritoneum, the starting point for separation of the peritoneum posteriorly.

Fig. 3. Rotation of cecum anteriorly, showing underlying tumor of the appendix. Allis forceps are on the unopened peritoneum.

Fig. 4. Peritoneum opened and appendix extruded.

Fig. 5. Removal of appendix.

Fig. 6. Showing type of appendix, hemorrhage into lumen, and fecalith.

[1]Sloan, LeRoy Hendrick. Practice of Medicine, Tice, Vol. VII, p. 631a. Hagerstown, Md.: W. F. Prior Co., Inc.

Fig. 1.

Fig. 2.

Fig. 3.

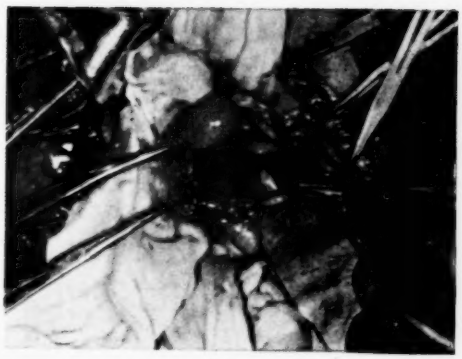

Fig. 4.

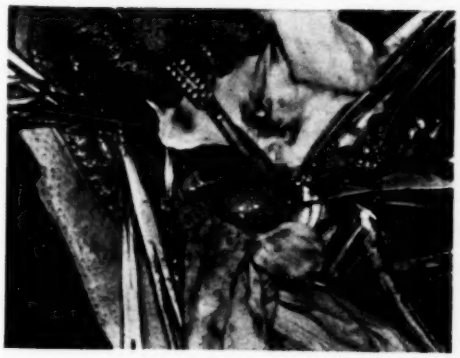

Fig. 5.

Fig. 6.

Retrocecal Appendix, Its Diagnosis and Surgical Approach.—William T. Harsha.

UNIV. OF MICH.

This peritoneum is now incised and the appendix is permitted to extrude itself. It can be gently aided if needed (Fig. 4). The presence of fecaliths with necrosis of the wall of the appendix in this position necessitates extreme care in handling at this point, as the appendix in this position is often friable (Fig. 5).

If an abscess cavity of limited area exists around the posterior cecal wall, the anterior margin of the peritoneum may be sutured to the posterolateral cecal wall or to the lateral cecal wall, exteriorizing from an abdominal point of view the infected area. If necrosis of the posterior wall of the cecum has occurred, it should be inverted by sutures. Into this area a Mikulicz drain is placed through a lumbar stab wound. The closure of this peritoneum is otherwise without drainage, and the wound is closed in layers with sutures of catgut.

SUMMARY

Acute retrocecal appendicitis may be recognized clinically by a vertical line of tenderness extending upward from the iliac crest, 6 to 8 centimeters posterolateral to the anterior superior spine, to the tip of the appendix, often below the rib margin.

The clinical course is often slower in development than other types, due to the relative absence of peritonitis.

A surgical approach to this retrocecal appendix which has proved of advantage is described.

THE TONUS OF THE UTERUS DURING PREGNANCY AND ITS RELATION TO LABOR

A Study of 1028 Observations Made With the Lóránd Tocograph

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OBSTETRICIANS have paid little attention to the hardness or tonus of the human uterus that is present between the intermittent contractions which occur during pregnancy. This has been due chiefly to the lack of a suitable means for measuring it. The development of the tocograph (1) however, has supplied such a need. It has demonstrated that tonus varies from patient to patient at identical periods during pregnancy, as well as in the same patient at different times.

It need hardly be mentioned that the character of labor varies likewise from patient to patient, and it is equally well known that we do not possess, at the present time, any means for predicting what the nature of the labor may be. These facts raised the question as to whether there might not be a significant correlation between the tonus of pregnancy and the character of the labor. If such were the case, the information resulting from a consideration of the relationship would have definite practical value; and if not, a study of tonus would at least throw some light upon a little understood characteristic of uterine physiology.

In previous communications (2, 3) we reported upon the variations in the tonus of the uterus which occur during pregnancy and labor. These observations were relatively few in number. Since they were published, additional ones have been made, which include the recording of some unusually high degrees of tonus. These facts, together with our desire to determine the exact relation between pregnancy tonus and the character of labor, have led to the present re-examination of all of our available material.

From the Gynecean Hospital Institute of Gynecologic Research, Department of Obstetrics and Gynecology, University of Pennsylvania.

MATERIALS AND METHODS

The observations were made between August, 1938, and April, 1941, upon patients attending the Maternity Department of the Hospital of the University of Pennsylvania, and ones residing in a private maternity home in Philadelphia.

Measurements of tonus were secured with a Lóránd tocograph which has been described fully elsewhere (1). In brief, however, it is a mechanical kymograph, which registers uterine movements through the medium of the abdominal wall.

Tonus is measured in the following manner: The clockwork of the tocograph is started, and the recording pen is allowed to draw a base line upon the recording paper before the machine is placed upon the patient. With the latter in the supine posture the tocograph is then placed upon the most prominent part of her abdomen.

If the uterus is relatively soft when the tocograph is placed upon the abdomen, the button projecting from the bottom of the machine buries itself full length in the abdominal wall, and thus the recording pen connected with the button fails to be dislodged from its base line position. Under these conditions, the patient is classified as exhibiting no increase in tonus (Fig. 1, *226*). Above a certain, yet unknown, degree of uterine tonus, the tocograph button meets sufficient resistance in the abdominal wall to displace it into the machine, thus dislodging the recording pen from its base line position. Under these conditions, the patient is classified as exhibiting an increase in tonus (Fig. 1, *1273*). The amount of the latter is estimated in terms of the distance traversed by the pen; under extreme circumstances this may reach a maximum of 25 millimeters. For a more detailed consideration of the condition represented by the term tonus, the reader is

Fig. 1. Illustrating the tocographic recording of nonmeasurable (low) and measurable (unusually high) uterine tonus during pregnancy. Tracing 226, patient a tripara. Record made day before onset of labor. Tocograph placed on abdomen at *A* and removed at *B*. Note absence of any shift of base line at these points. Tonus nonmeasurable. Tracing 1273, patient a tripara. Record made day before onset of labor. Tocograph placed on abdomen at *A* and removed at *B*. Note elevation of base line between these two points. Tonus measurable and quite high (13 mm.).

referred to the evaluation which appears at the end of this report.

RESULTS

A group of 435 patients supplied a total of 1,028 tocographic records. These were secured from the 79th day of pregnancy to the day before labor, inclusive. The number of records per individual appears in Table I. The observations are presented under two headings: (1) "Tonus in Relation to Pregnancy," and (2) "Tonus in Relation to Labor."

Tonus in relation to pregnancy. In a selected group of individuals recordings were made at regular intervals. Table II shows the incidence of tonus and its degree in 15 patients who were observed at weekly intervals throughout the 9 or more weeks immediately preceding labor. A measurable increase in tonus occurred rarely before the 33rd week of gestation; even after that time, both the incidence and degree varied widely. Patient 14 registered no increase at any time before the onset of labor. In contrast to her, patient 6 exhibited measurable tonus as early as the 30th week, and practically every week thereafter. Patient 4 showed no tonus until the last week of gestation.

The presence of measurable tonus at any one time was no indication that it would be found at the time of subsequent recordings, though such was more likely to be the case. These data emphasize the variability with which a measurable increase in tonus appears in the same person from week to week, and in different persons at the same period of gestation.

In an unselected group of individuals recordings were made at irregular intervals (Tables III, IV, and V).

The influence of advancing pregnancy upon the incidence of a measurable increase in tonus is given in Table III which lists the percentage of tocographic tracings registering a measurable amount of tonus, arranged according to gravidity and to the time in pregnancy that they were secured. This degree of tonus was observed in primigravidas as early as the 6th lunar month of pregnancy, but not until the 7th month in the case of multigravidas. Primigravidas exhibited their first significant increase in the incidence of measurable tonus, during the 8th month, whereas multigravidas did not do so until one month later. During the 10th lunar month, 58.6 per cent of tracings of primigravidas showed an increase in tonus, in contrast to 37.9 per cent of observations upon multigravidas. Thus, only 48.4 per cent of tracings of primigravidas and multigravidas combined, recorded a measurable increase in tonus during even the last month of gestation.

The influence of advancing pregnancy upon the degree of increase in tonus is recorded in Table IV which shows the average and maximum amount of tonus observed in the tracings of those patients who exhibited a measurable increase in tonus. The degree of tonus increased progressively as pregnancy ad-

TABLE I.—TOCOGRAPHIC RECORDS PER INDIVIDUAL

Tocographic records	Individuals
1	272
2	74
3	29
4	18
5	6
6–10	18
11–15	11
16–20	4
21–25	3
Total	435

TABLE II.—INFLUENCE OF PREGNANCY UPON UTERINE TONUS

Duration of gestation in weeks	Uterine tonus: Patient identification														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
16	0														
17	0														
18	0	0													
19	0	0													
20	0	0													
21	0	0	0												
22	0	0	NT												
23	0	0	0												
24	0	0	2	0											
25	0	0	0	0	0										
26	0	0	0	NT	0										
27	0	0	0	0	0	0									
28	0	0	0	0	0	0	0	0							
29	0	0	0	0	0	0	0	1	0	0					
30	0	0	1	0	0	1	0	0	0	NT	0	0			
31	0	0	0	0	0	8	0	0	0	0	0	0			
32	0	2	0	0	0	0	0	2	0	0	0	0	0	0	0
33	0	7	0	0	0	5	2	0	0	2	NT	0	0	0	0
34	0	2	0	0	0	3	0	0	0	1	3	0	0	0	NT
35	4	4	2	0	0	1	0	3	0	0	0	2	0	0	0
36	4	0	0	0	0	2	0	NT	1	0	1	0	1	0	0
37	2	0	0	0	2	6	0	1	6	NT	2	0	0	0	0
38	0	0	0	0	1	7	3	2	1	6	2	NT	0	0	NT
39	7	0	0	0	2	2	1	3	1	0	1	0	0	0	0
40	7	4	0	5	1	4	6	8	5	4	1	0	0	0	1

Table II. Showing influence of advancing pregnancy upon incidence and degree of measurable tonus in 15 patients who were studied at weekly intervals for the 9 or more weeks immediately preceding labor. *O* Indicates absence of measurable tonus. Other numerals represent measurable tonus expressed in millimeters. *NT* Stands for "no tracing." Note: (a) Definite increase in the number of tracings showing measurable tonus after the 32nd week of pregnancy; (b) variability both in occurrence and in degree of tonus in same patient from week to week, and in different individuals at the same period of pregnancy; (c) generally increased tonus during the 40th week, although some patients exhibited no measurable tonus at this time.

vanced. By the end of pregnancy, however, the amount of tonus was practically identical in primigravidas and multigravidas.

The influence of the last 14 days of pregnancy upon uterine tonus is shown in Table V which

TABLE III.—INFLUENCE OF ADVANCING PREGNANCY UPON UTERINE TONUS

Lunar month of pregnancy	Tocographic records of: Primigravidas and multigravidas			Primigravidas			Multigravidas		
	Records	Showing increase in tonus		Records	Showing increase in tonus		Records	Showing increase in tonus	
		No.	%		No.	%		No.	%
3rd	1	0	0.0	0	0	0.0	1	0	0.0
4th	2	0	0.0	2	0	0.0	0	0	0.0
5th	13	0	0.0	9	0	0.0	4	0	0.0
6th	24	1	4.2	19	1	5.3	5	0	0.0
7th	67	2	3.0	38	1	2.6	29	1	3.4
8th	84	12	14.3	70	12	17.1	14	0	0.0
9th	190	61	32.1	124	49	39.5	66	12	18.2
10th	647	313	48.4	328	192	58.6	319	121	37.9

Table III. Showing the influence of advancing pregnancy upon the frequency with which measurable tonus was observed in 1,028 tocographic tracings, arranged according to gravidity. Note: (a) Absence of measurable tonus prior to the 6th lunar month in the case of primigravidas, and prior to the 7th month in multigravidas; (b) progressive increase in incidence of measurable tonus as pregnancy advances; (c) absence of measurable tonus during the last month of pregnancy in more than half of the tracings; (d) greater frequency of measurable increase in tonus throughout pregnancy in primigravidas than in multigravidas.

TABLE IV.—INFLUENCE OF ADVANCING PREGNANCY UPON UTERINE TONUS

Lunar month of pregnancy	Records showing an increase in tonus: Primigravidas			Multigravidas		
	Records	Tonus		Records	Tonus	
		Average	Maximum		Average	Maximum
		mm.	mm.		mm.	mm.
6th	1	1.5	1.5	0	0.0	0.0
7th	1	1.0	1.0	1	1.5	1.5
8th	12	2.4 ± 2.4	8.0	0	0.0	0.0
9th	49	3.9 ± 3.6	15.0	12	3.9 ± 2.7	8.0
10th	192	4.3 ± 3.1	16.0	121	4.1 ± 3.4	15.0
Total	255			134		

Table IV. Showing the influence of advancing pregnancy upon the degree of tonus observed in 389 tocographic records which registered a measurable increase. Note: (a) Progressive increase in the degree of tonus as pregnancy advances; (b) absence of any significant effect of gravidity upon degree of tonus even during the last month of pregnancy.

TABLE V.—INFLUENCE OF LAST 14 DAYS OF PREGNANCY UPON UTERINE TONUS

Days before labor	Primigravidas and multigravidas			Primigravidas			Multigravidas		
	Total records	Tonus increased		Total records	Tonus increased		Total records	Tonus increased	
		Records	Average increase		Records	Average increase		Records	Average increase
			mm.			mm.			mm.
14	16	8	2.9	7	4	3.9	9	4	1.8
13	25	9	2.2	16	8	2.3	9	1	1.0
12	17	8	3.4	6	4	3.7	11	4	3.0
11	21	8	4.4	14	6	5.3	7	2	1.5
10	23	5	3.8	15	3	4.3	8	2	3.0
9	27	12	4.8	13	7	3.6	14	5	6.5
8	32	17	3.0	13	8	2.7	19	9	3.2
7	24	13	3.9	13	10	3.6	11	3	5.1
6	32	15	5.8	14	8	4.9	18	7	6.9
5	30	19	3.8	9	7	3.3	21	12	4.1
4	28	15	5.4	16	13	5.7	12	2	3.4
3	26	12	2.8	15	8	3.0	11	4	2.5
2	50	34	5.0	25	22	5.6	25	12	3.8
1	100	60	5.2	44	32	4.9	56	28	5.6

Table V. Showing the influence of the last 14 days of pregnancy upon the incidence and degree of measurable tonus as observed in 451 tocographic tracings. Note: (a) Relatively constant occurrence of measurable tonus; (b) the slight but gradual increase in degree of tonus; (c) the absence of any abrupt change in tonus; (d) the absence of any effect of gravidity upon either characteristic.

gives: (a) the number of tocographic tracings made during the last 14 days of pregnancy, (b) the number of these which registered a measurable increase in tonus, and (c) the average increase in the latter group. The data in this table indicate: (a) the marked variability in the incidence of measurable tonus at this time and also (b) the similar variability in the degree of increase. Furthermore, they show that no sudden change in either characteristic takes place at this time, although there was a tendency for the tonus to become stabilized during the few days immediately preceding labor.

Tonus in relation to labor. Table VI shows the influence of tonus, registered during the last 4 weeks of pregnancy, upon the duration of labor of primigravidas. Each record represented a different patient; no individual exhibited any evidence of cephalopelvic disproportion; all deliveries were vaginal; the infants had cephalic presentations and weighed between 2,500 and 3,500 grams at birth.

The data in the two left-hand columns of Table VI were supplied by patients exhibiting no measurable increase in tonus. Patients who registered a measurable increase supplied the information in the right-hand columns.

The average duration of labor of the patients whose tonus was above the average of those who exhibited measurable tonus did not differ significantly from that of the patients who recorded no measurable tonus at the same periods of pregnancy, respectively.

Table VII shows the influence of tonus, upon the duration of labor of multigravidas. As in the case of primigravidas, the amount of tonus present during late pregnancy had no influence upon the duration of labor.

As to the influence of an unusually high tonus during the last week of pregnancy upon the duration of labor the following is recorded: Eight primigravidas experienced an unusually high degree of tonus (10 to 17 millimeters). One (tonus 15 millimeters) gave birth to a 4,500 gram infant by forceps after a prolonged

TABLE VI.—INFLUENCE OF TONUS UPON DURATION OF LABOR

Primigravidas

Week of pregnancy	Tonus			
	Not recordable		Above average	
	Number of records	Average duration of labor	Number of records	Average duration of labor
		Hours		Hours
37th	16	16.9	5	12.8
38th	16	14.5	4	10.1
39th	24	14.4	6	8.8
40th	23	13.5	18	14.2
Wt. Av.	..	14.8	..	12.5

Table VI. Showing the average duration of labor of a group of primigravidas from whom tocographic records were secured during the last 4 weeks of pregnancy, arranged according to whether measurable tonus was absent, or above the average in the group that exhibited measurable tonus. Note that the average duration of labor was slightly shorter in the group which exhibited a tonus above the average. Compare with data in Table VII.

TABLE VII.—INFLUENCE OF TONUS UPON DURATION OF LABOR

Multigravidas

Week of pregnancy	Tonus			
	Not recordable		Above average	
	Number of records	Average duration of labor	Number of records	Average duration of labor
		Hours		Hours
37th	13	7.5	3	7.9
38th	20	8.5	9	13.0
39th	27	8.7	12	12.0
40th	47	7.8	27	7.2
Wt. Av.	..	8.1	..	9.4

Table VII. Showing the average duration of labor of a group of multigravidas from whom tocographic records were secured during the last 4 weeks of pregnancy, arranged according to whether measurable tonus was absent or above the average in the group that exhibited measurable tonus. Note that the average duration of labor was shorter in the group which recorded *no* measurable tonus. Compare with data in Table VI.

second stage. Another, with a tonus of 17 millimeters was delivered by cesarean section on account of cephalopelvic disproportion and primary inertia. A third patient had a breech delivery. The 5 remaining delivered spontaneously, only 1 having a slightly prolonged second stage.

Five multigravidas also registered an unusually high degree of tonus (10 to 13 millimeters) during the last week of pregnancy. The labors of all were short; no second stage lasted longer than 45 minutes; 3 of the deliveries were precipitous.

There was no evidence to indicate that the high tonus of any patient influenced adversely the course of labor. If it had any appreciable effect whatever, it aided rather than retarded delivery.

EVALUATION OF STUDY

The present observations indicate that, within certain limits, tonus can be measured with a satisfactory degree of accuracy during pregnancy. This statement is based upon (a) repeated observations upon the same individual at intervals of hours, days, weeks and months, and (b) by comparing repeated observations upon one individual with those of another. Uniform results have been secured from individuals who varied considerably both in weight and in the thickness of their abdominal walls. In carrying out the measurement, the tocograph usually is placed in the midline and above the umbilicus, where the abdominal wall is relatively thin and in close contact with the upper pole of the uterus. Furthermore, the registering of the tonus is not influenced by the tightness of the belt which holds the tocograph in position, since varying this factor has no influence upon the measurement.

Although the method of measurement is satisfactory, it is not fully established as to just what is being measured. Wolf, who has compared measurements made with intrauterine bags with those secured by external hysterography, concludes that the latter records the hardness of the uterine wall rather than intrauterine pressure. The present author concurs in this belief. Whichever characteristic the measurement represents, it is certainly only relative, but nevertheless useful as a means for comparing one patient with another.

It is apparent that tonus varies considerably during pregnancy, but no evidence is forthcoming as yet to explain why these variations occur.

It is an interesting observation that a measurable increase in tonus occurs earlier in primigravidas than in multigravidas, and that more of the former experience it throughout pregnancy than do the latter. On the other hand, the degree of tonus attained at the end of pregnancy appears to be the same in primigravidas as in multigravidas. One might expect it to be higher in primagravidas at this time, in view of the fact that it appears earlier and more often in them than it does in the multigravidas.

There appears to be an unusual increase in the incidence of measurable tonus during the 8th lunar month of pregnancy, but no significant change in it during the 2 weeks immediately preceding the onset of labor. It follows from this that knowledge of the degree of tonus present just before labor is of *no* aid in predicting the time of onset of labor. Nor has any evidence come to light to indicate that a study of tonus alone is of any value in predicting the quality of the uterine activity at the time of labor.

The methods employed in securing the present data have their obvious limitations. These include the fact that the tocograph has the inherent weakness of any precision instrument operated by a spring; that the present observations were made by several different individuals, who employed a number of different tocographs. It is believed, however, that some of the difficulties encountered are out-weighed by the number of observations made.

SUMMARY AND CONCLUSIONS

1. A series of 435 patients supplied 1,028 tocographic records of what, for want of a better term, may be described as uterine tonus during pregnancy.

2. Detectable increases in tonus were observed first in primigravidas during the 6th lunar month, and not until the 7th month in the case of multigravidas.

3. Wide variations in tonus were observed in the same patient at different times during pregnancy and in different individuals at similar periods of gestation.

4. Tonus increased progressively in degree as pregnancy advanced, in those patients who exhibited a measurable amount.

5. An unusual increase in tonus appeared in primigravidas during the 8th month, but not until the 9th month in the case of multigravidas.

6. Although primigravidas experienced increases in tonus earlier and more often in pregnancy than did multigravidas, the ultimate level of their tonus did not exceed that of the multigravidas.

7. During the last lunar month of pregnancy, less than half of all patients exhibited any measurable tonus.

8. From these observations, it is concluded that knowledge of the uterine tonus present during pregnancy is of no value in predicting either the time of onset of labor or its character.

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THE FUNCTIONAL ANATOMY OF LABOR AS REVEALED BY FROZEN SAGITTAL SECTIONS IN THE MACACUS RHESUS MONKEY

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UNTIL recently our concepts concerning the action of the human uterus were based almost wholly upon principles which were developed nearly half a century ago. These principles arose from two general sources: first, clinical observation of the laboring uterus, and second, studies of frozen sagittal sections of women who had died in labor. A relatively large number of human frozen sections have been made and their study has contributed much to our knowledge. However, the sections have been made under such varying circumstances, in regard to the cause of death and the type of labor, as to engender skepticism concerning their true representation of the normal process. The freezing methods were slow and in some instances the specimens were not frozen until a number of days after death.

Since the evidence obtained by the frozen-section technique is essential for a thorough understanding of the process of evacuation of the uterus, our work was undertaken to obtain such evidence under uniform conditions as to the cause of death and the time and method of freezing. It was believed that the possession of such evidence for the uterus of a subhuman primate would supplement and render it possible to evaluate more accurately the evidence supplied by the human specimens.

In this study rather extensive chronological evidence of the anatomicophysiological changes occurring in the laboring monkey uterus has been obtained. The Macacus rhesus was chosen as a suitable subject because of our familiarity with the uterus of this animal, because of its close anatomical and physiological similarity to the human uterus, and because certain points of evidence required could never be obtained in the human being. Of course, results obtained in one species must be applied to another with reservation. However, our knowledge of the gross, comparative, and functional anatomy of the rhesus uterus indicates that the processes concerned in evacuation should be fundamentally the same in both species.

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ANATOMICAL CONSIDERATIONS

Before considering our own data, it is important to obtain a clear understanding of the anatomical divisions of the nonpregnant uterus, and their fate in early pregnancy. These points are stressed, first, because they are essential to an adequate understanding of the subject which we wish to present, and, second, because they are not generally used despite their thorough and adequate demonstration.

Until the early part of the present century the human uterus was considered as being composed of two essential parts: cervix and corpus. The term "isthmus" had been employed upon occasion, but it was not until the work of Aschoff in 1905 that the isthmus was seen to be a definite structure, distinct from both cervix and corpus, anatomically as well as functionally. Since this time the subject has been considered by numerous authors, the overwhelming majority of whom subscribe to Aschoff's observations. The work of Stieve, in 1927, has emphasized and extended the observations of Aschoff, and now serves as the classic description of cervix and isthmus uteri and their intrinsic changes in pregnancy, labor, and the puerperium. In addition to these, the comprehensive article by Frankl is most valuable.

The uterus is now considered as being composed of 3 essential parts: the cervix, isthmus, and corpus. The cervix and corpus require no description in this communication.

When the uterine cavity is examined in a frontally sectioned uterus, the cavum corporis is seen to terminate inferiorly by a narrow canal, which soon widens into the spindle-shaped canal of the cervix proper. The length and structure of this canal varies in different specimens, and with parity. Ordinarily it is approximately 6 to 10 millimeters in length, and slightly narrower at its superior extremity. In many specimens the lower extremity can be distinguished grossly, but in others the canal terminates gradually in the cervical lumen. It is to the tissue which surrounds this canal, throughout the thickness of the uterus, that the term *isthmus* has been applied. The upper limit of the isthmus, the "*anatomical* internal os," is discernible with the naked eye. It is a definite muscular constriction which is often referred to, inadequately, simply as the "internal os." Aschoff adds that "at this point, where there is distinguishable externally a slight constriction, where as a rule there is the tight adhesion of the peritoneum, and where the first large transverse branches of the uterine artery enter the muscle substance, lies the upper limit of the isthmus." Again, to quote Aschoff, the lowermost extent of the isthmus uteri, the so called "*histological* internal os," is the "line of demarcation between the (columnar) epithelium of the cervical canal and the corporeal epithelium, but not, as is so often said, the upper limit of the arbor vitae. The fold formation cannot be used in the determination of the line of demarcation. Furthermore, here the cervical and corporeal glands mingle." The transition from cervix to isthmus is therefore a gradual one, which occurs over the course of 1 or 2 millimeters or more. Frankl states that with experience this transition is often distinguishable grossly.

Structurally, the isthmus resembles the corpus, but there are certain essential differences. The mucosa is thinner than that of the corpus, is richer in supporting tissue, and poorer in glands. The musculature is more poorly developed than that of the corpus, better so than that of the cervix.

The following changes are reported during pregnancy. Until the end of the second month the canal of the isthmus remains narrow, but it lengthens considerably, up to 2 to 3 times its former length. (It is of incidental interest that when a vaginal hysterotomy is performed at this stage of pregnancy one might, unless cognizant of these isthmic changes, attribute the greatly increased distance from external os to ovum chamber as being due solely to an increase in the length of the cervix. Stieve's investigations show quite clearly that there is no significant increase in cervical length. The increased distance from anatomical internal os to external os is due almost entirely to lengthening of the isthmus.) In the third month the wall of the isthmus unfolds quite rapidly, and the canal widens to form a part of the general uterine cavity. From this time until the conclusion of pregnancy, the boundary between the general uterine cavity and the cervical canal is the histological internal os of Aschoff, which now becomes known clinically as the *obstetric internal os* (O. I. O.). (This differentiation is important, since it emphasizes the inadequacy of the unqualified term "internal os"). At term the isthmus uteri measures from 7 to 10 centimeters in length, thus making up between one fifth and one fourth of the total sagittal length of the uterus.

The nonpregnant monkey uterus. Three nonpregnant rhesus uteri have been studied. A section of one of these is shown in Figure 1. The major difference between the rhesus and human uterus is the cervical canal, which is straight in the latter, tortuous in the former. The tortuosity of the rhesus cervical canal is due to the presence of nipple-like projections (colliculi) from the walls of the cervix. Our findings concerning the location of these colliculi are not entirely in agreement with those reported by other workers and will be considered in detail in a later communication. Briefly, in all of the specimens studied we have observed 4 such projections, the 2 uppermost of which we have termed the internal lips of the cervix, the 2 lowermost, the external cervical lips. Histological examination of the nonpregnant specimens indicates that the cervical canal extends from the ex-

ternal cervical lips to a point on the upper aspect of the internal lips. The isthmus appears to extend from this latter point upward for a distance of 8 to 10 millimeters. The remainder is corpus.

It is of interest that a physiological sphincter exists in the rhesus uterus at the junction of cervix and isthmus (at the site of the obstetric internal os). This can be felt to contract about the examining finger, and balloon records can be made of its activity (Ivy, Hartman and Koff; Danforth and Ivy).

Changes in the monkey uterus during pregnancy. No sections during early pregnancy are included in our series of animals. The work of Franke upon an allied species ("Cercocebus cynomorpha"), however, serves to fill this gap. Despite the fact that his work was done before the demonstration of the isthmus uteri, Franke's careful descriptions leave little doubt of the fate of this structure during early pregnancy. According to his observations, the isthmus in this species unfolds and the canal widens in a manner which is essentially similar to that described for the human being. After the widening occurs, the junction between the uterine cavity and the cervix is at the level of the internal lips of the cervix. This latter is in agreement with our findings. Thus, the internal lips definitely mark the obstetric internal os anatomically so that it may be followed throughout labor.

METHODS

Thirty-three Macacus rhesus monkeys were studied. Three were nonpregnant controls. Three were sacrificed late in pregnancy, prior to the onset of labor. Six were sacrificed at various stages from the onset of labor to complete effacement and dilatation of the cervix. Sixteen were sacrificed during the second stage of labor, 1 during the third stage, and 4 at various intervals from 1 hour to 1 week postpartum.

The descriptions by Hartman and by Hartman and Straus were found to be most helpful in the diagnosis of labor in the early animals of this series, and in the handling and care of all the animals.

The progress of labor was followed by abdominal palpation and digital vaginal examination. When the desired stage of labor was reached, the animal was lightly anesthetized with intravenous sodium pentobarbital. This drug did not inhibit the uterine contractions perceptibly. The anesthetized animal was fastened by light cords to a rectangular metal frame which maintained a modified lithotomy position. At the height of a uterine contraction the animal was lowered into the freezing chamber.

The freezing solution was kept ready for immediate use. The chamber consisted of an insulated, galvanized iron tank containing a mixture of 95 per cent ethyl alcohol and chipped dry ice (solid carbon dioxide). After a period of time this mixture reaches a temperature of −70 to −80 degrees C., and maintains itself there until all the dry ice has vaporized.

While freezing, the animals were kept completely submerged. They were allowed to remain in the chamber for at least one hour so that they reached the temperature of the freezing mixture.

By means of a motor driven band saw with a movable platform, the upper abdomen, tail and lower legs were removed, and a median sagittal section of the remaining torso was made. The cervix was cleanly bisected in all instances.

While in the frozen state direct outline tracings of the sections were made and measurements taken, both the specimens themselves and the tracings being utilized. Precise pen and ink drawings were prepared by the artist from the direct tracings. Wash drawings were prepared from the specimens in order to illustrate certain points of detail which were not apparent in the pen and inks. In each of the frozen specimens, a section was made one half inch lateral to the midline. This half inch slice was placed in 10 per cent formalin, and from it histological sections of the uterus were made. These are not reported here, except in so far as they are necessary for the confirmation of results.

Of the 33 specimens available, 11 representative ones have been selected for reproduction at this time.

In regard to the measurements, it is emphasized that it is our purpose not to present a rigid statistical analysis of labor, but rather to gain knowledge of the general trends in labor. The variation in measurements of this type is considerable, and the possible ways of measuring the same structure are legion. In order that variations might be reduced to a minimum, all measurements were made by the same individual utilizing precisely the same technique in all specimens. All measurements were verified at least twice. It is perhaps unnecessary to point out that rigid statistical treatment of results such as these is a meaningless procedure.

The following measurements and ratios are presented at this time:

1. The total internal sagittal circumference of the uterus.

2. The greatest length from the internal aspect of fundus to plane of external os.

TABLE I.—EXAMPLE OF COMPLETE LABOR PROTOCOL, MONKEY NO. 14 (SERIES NO. 8) DATE: MAY 19, 1938

Time	Remarks
7:15 p.m.	Animal lay down, appeared somewhat more nervous than usual. Her face was flushed in a manner similar to that of previously observed laboring monkeys.
7:25 p.m.	Vaginal examination: Cervical dilatation 1.5 cm. Contractions of fairly good quality, occurring every 2 to 2½ minutes, lasting 30 to 35 seconds. Forewaters bulging through cervix with each pain.
7:30 p.m.	Animal tied down to allow precise observation.
8:45 p.m.	Vaginal examination: Findings essentially the same as noted above.
8:50 p.m.	Animal allowed up in cage.
9:00 p.m.	More restless with pains.
9:10 p.m.	Vaginal examination: Cervix partially effaced, dilated 2 cm. Pains of good quality, occurring every 2 to 2½ minutes and lasting 35 to 40 seconds.
9:25 p.m.	Vaginal examination: Cervix fairly well effaced, dilated 2 to 2.5 cm. Head entering the pelvis.
9:30 p.m.	Anesthetized.
9:35 p.m.	Freezing started. Temperature of the bath −72 degrees C.
10:35 p.m.	Animal removed from freezing mixture.

3. Relation of the cervical lips to the anatomical conjugate, to the symphysis, and to the promontory of the sacrum. (In this report the term true conjugate is used synonymously with anatomical conjugate, to indicate the distance from the superior edge of the symphysis to the sacral promontory. It is to be distinguished from the obstetrical conjugate which is the shortest distance from the symphysis to the promontory.)

4. Sagittal circumference of the uterine cavity from obstetrical internal os anteriorly to obstetrical internal os posteriorly.

5. Total length of the cervix.

6. Sagittal circumference of the uterus below the insertion of the placenta, or below a retraction or constriction ring.

For purposes of comparison all of the published human frozen sagittal sections were subjected to similar, though necessarily less exact, measurement. These are not included in the present report, except to indicate certain points of similarity.

RESULTS

In the discussion of results, the first and third stages of labor have been considered in accordance with the usual definitions, respectively, from the onset of labor until complete dilatation of the cervix, and from delivery of the babe until after the birth of the placenta. For purposes of description it has been found advisable to divide the second stage into 3 substages, rather than to consider it as a whole as is customary. Substage II A has been used to designate the changes occurring from the time of complete dilatation until separation of the lower border of the placenta occurs (*v.i.*). Substage II B has been used to indicate the changes occurring from the time of separation of the lower border of the placenta up to, but not including, the birth of a part. Substage II C includes the changes from the birth of a part to the birth of the entire fetus. These substages are clearly evident in our sections.

An example of a complete labor protocol is shown in Table I.

TABLE II.—SHOWING (1) THE RELATION OF THE TOTAL INTERNAL CIRCUMFERENCE (A) TO THE LENGTH FROM THE INNER ASPECT OF THE FUNDUS TO THE PLANE OF THE EXTERNAL OS (B), AND (2) THE RELATION OF INTERNAL CIRCUMFERENCE FROM O.I.O. TO O.I.O. (C), TO THE LENGTH FROM INTERNAL FUNDUS TO PLANE OF O.I.O. (D).*

Stage	Total circumference E.O. to E.O. A	Greatest length fundus to plane of E.O. B	Ratio B÷A	Total circumference O.I.O. to O.I.O. with lips C	Greatest length fundus to plane of O.I.O. with lips D	Ratio D÷C
Before labor (term?) (Cases 1–3)	36.4	14.5	40.0	35.0	14.4	41.1
I (Cases 5–9)	43.3	17.4	40.1	41.0	16.1	40.0
II A (Cases 10–12)	34.9	14.4	41.5	31.7	12.9	40.7
II B (Cases 13–19)	30.1	12.3	40.8	27.4	11.0	40.1
II C (Cases 20–25)	26.1	11.0	42.1	22.5	8.6	38.2
III	18.5	7.2	39.0	17.3	6.8	39.3
P.P.—1 hour to 3 days	18.1	7.6	40.3	15.3	6.2	43.8
P.P.—1 week	15.0	6.7	44.6	12.9	5.8	44.9
Nonpregnant	9.1	4.4	48.3	6.7	3.2	47.7

O.I.O., obstetric internal os; E.O., external os.

*Since the internal circumference is obviously irregular, the extent of the accuracy of the measurements may be subject to question. This problem can be tested by ascertaining whether the circumference bears a rather constant ratio to the length or long diameter of the uterus which is roughly an elipsoid. The ratios are surprisingly constant, and prove the relative accuracy of the method of measurement. Measurements in this table, as in others, are in centimeters.

TABLE III.—THE RELATION OF THE CERVICAL LIPS TO THE ANATOMICAL CONJUGATE, TO THE LEVEL OF THE SYMPHYSIS, AND TO THE LEVEL OF THE PROMONTORY

Stage	Lips as related to anatomical conjugate				Lips as related to symphysis				Posterior lips as related to sacral promontory	
	Anterior		Posterior		Anterior		Posterior			
	External	Internal	External	Internal	External	Internal	External	Internal	External	Internal
Before labor (term?)	−2.4	−2.1	−2.5	−2.0	−0.1	+0.6	+0.2	+1.0	−4.9	−4.1
I	−2.7	−2.3	−3.1	−1.8	−0.6	−0.2	0	+1.7	−5.5	−3.9
II A	+1.4	+1.6	−1.4	+0.7	+1.5	+1.8	+2.3	+5.0	−2.6	+1.2
II B	+1.5	+2.5	−0.1	+1.6	+1.7	+2.7	+4.0	+5.5	−0.4	+1.0
II C	+1.7	+2.4	−0.2	+1.6	+2.2	+3.2	+3.8	+5.7	0	−0.7
III	−1.3	−1.3	−0.6	+0.2	−0.3	−0.1	+3.5	+4.2	−1.0	−0.2
P.P. 1 hour to 3 days	−2.1	−1.8	−3.4	−2.0	−0.3	+0.3	−1.4	+0.6	−5.9	−4.0

− =Centimeters below structure in question.
+ =Centimeters above structure in question.

Of the 30 specimens during labor, illustrations of 10 have been selected for reproduction at this time, as representative of the changes which have been observed. These are the following:

1. (Monkey 4, Series 6) Questionable early labor. Dilatation 1 cm. by vaginal examination. (Figs. 2 and 2a.)

2. (Monkey 14, Series 8) See Table I. (Figs. 3 and 3a.)

3. (Monkey 19, Series 9) In labor 1 hour and 45 minutes. Dilatation 4 cm. by vaginal examination. Forewaters protruding through external os. (Figs. 4 and 4a.)

4. (Monkey 30, Series 12) Duration of labor unknown. First vaginal examination revealed complete dilatation. Sacrificed immediately. (Figs. 5 and 5a.)

5. (Monkey 21, Series 16) In labor about 10 hours. Head upon the perineum. (Figs. 6 and 6a.)

6. (Monkey 10, Series 19) In labor 1 hour and 15 minutes. Bearing down with pains for about 25 minutes. Face at the vaginal introitus. (Figs. 7 and 7a.)

7. (Monkey 23, Series 20) Duration of labor unknown. Animal suddenly seen to be bearing down. After a period of observation, she was sacrificed immediately after delivery of the head. (Figs. 8 and 8a.)

8. (Monkey 22, Series 23) In labor 4 hours and 15 minutes. Sacrificed after delivery of head and thorax (Figs. 9 and 9a.)

9. (Monkey 31, Series 26) Sacrificed immediately after delivery of stillborn baby after labor of unknown duration. Placenta *in utero*. (Figs. 10 and 10a.)

10. (Monkey 3, Series 27) Precipitate labor. Sacrificed 1 hour after delivery of placenta. (Figs. 11 and 11a.).

The figures presented in Tables II to VII are averages for all specimens in the par-

TABLE IV.—REDUCTION OF THE INTERNAL CIRCUMFERENCE OF THE UTERUS WITH THE PROGRESS OF LABOR

Stage of labor	No. of cases	Circumference cm. O.I.O. to O.I.O. with lips	Reduction (cm.) C	% Reduction C÷A	Circumference cm. O.I.O. to O.I.O. without lips A—B	Reduction (cm.)	% Reduction	Total length of both internal lips B
Before labor (term?)	3	35.0			32.8			2.2
I	5	41.0(A)			39.1			1.9
II A (up to separation of placenta)	3	31.7	9.3	22.7	30.4	8.7	22.2	1.3
II B (from some separation to birth of a part)	7	27.4	13.6	33.4	26.3	12.9	33.0	1.1
II C (after birth of a part)	6	22.5	18.5	45.0	21.3	17.8	45.5	1.2
III (placenta in uterus)	1	17.3	23.7	58.0	14.4	24.7	63.1	2.9
P.P. 1 hour to 3 days	3	15.3	25.7	62.7	13.3	25.8	66.0	2.0
P.P. 1 week	1	12.9	28.1	68.5	11.9	27.2	69.8	1.0

ticular group indicated. All measurements were made from the sagittal surface only. It is regretted that lack of space prevents the publication of all of the measurements at this time, and that only averages of the entire stages may be presented. Trends which are apparent within the stages are thus not evident, except for those which are illustrated in the graph which is included. Certain of these trends will be mentioned, then, without presentation at this time of the evidence which substantiates them. Also, in order to conserve space, the ranges of the figures used in computation of the averages are not included in this communication. The figures are sufficiently constant that the authors ascribe definite trend significance to them.

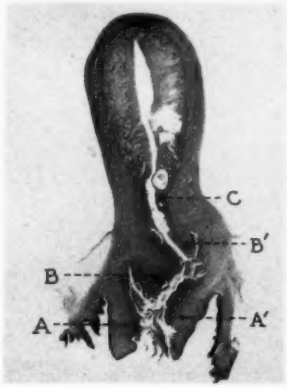


Fig. 1. Sagittal section of adult nonpregnant rhesus uterus, (1:1). *A,A'*, external cervical lips; *B,B'*, internal cervical lips; *C*, upper boundary of isthmus uteri.

ANALYSIS OF STUDY

The problem of precise differentiation of the fate of the various uterine segments in frozen sections of the human uterus offers difficulty because of the absence of gross fixed landmarks in this species. After dilatation of the cervix has started there is no definite means of determining the upper boundary of the cervix. The bladder reflection, commonly stated as being a rather definite indication of the upper limit of the isthmus, has been found to be of no value in the instance of the human frozen sections. Similarly, this point has been most disappointing as a landmark in the monkey

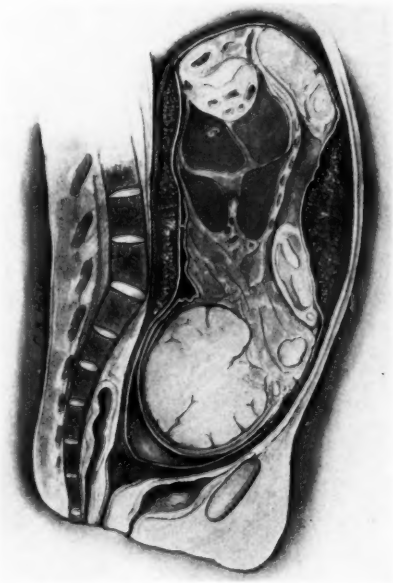


Fig. 2.

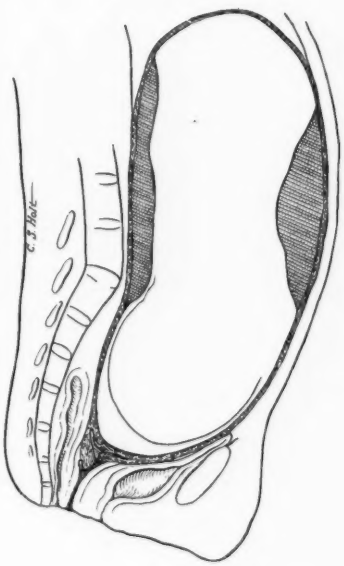


Fig. 2a.

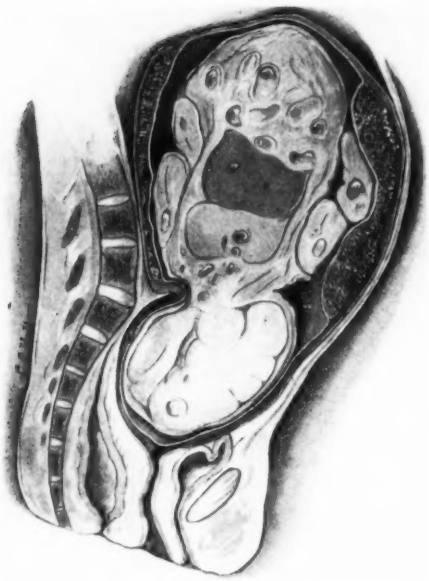
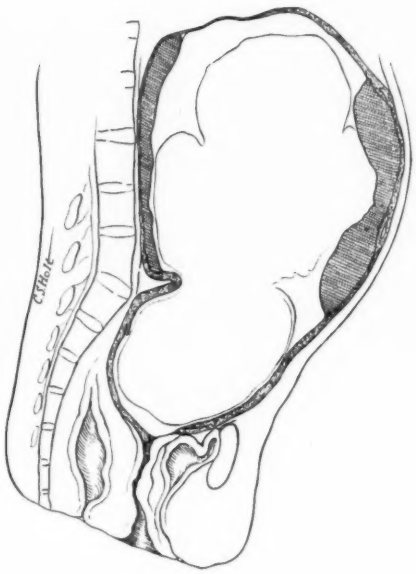


Fig. 3.



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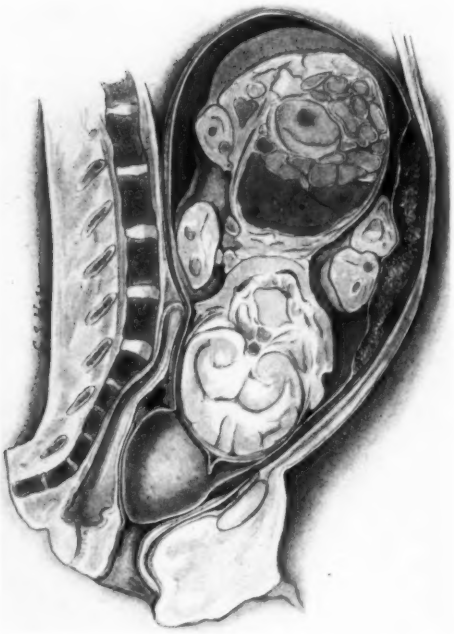

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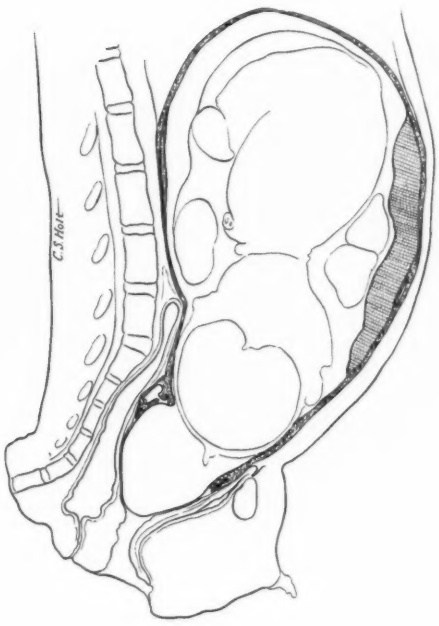

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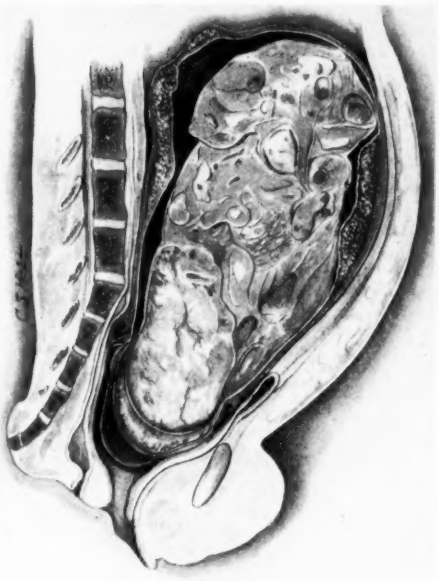

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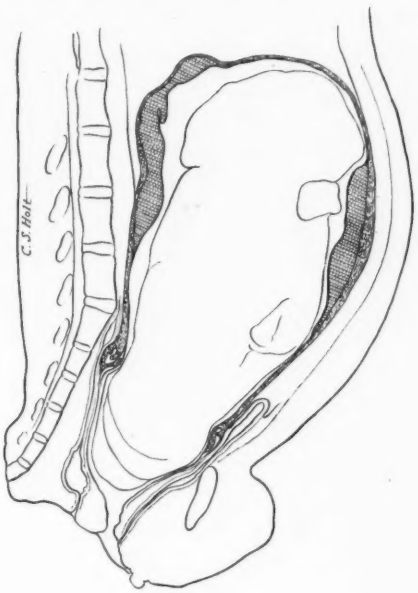

Fig. 5a.

Fig. 6.

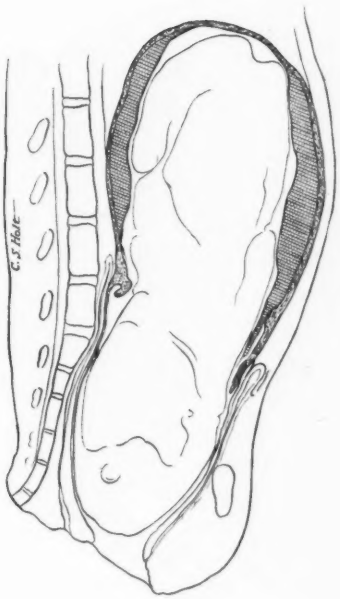

Fig. 6a.

Fig. 7.

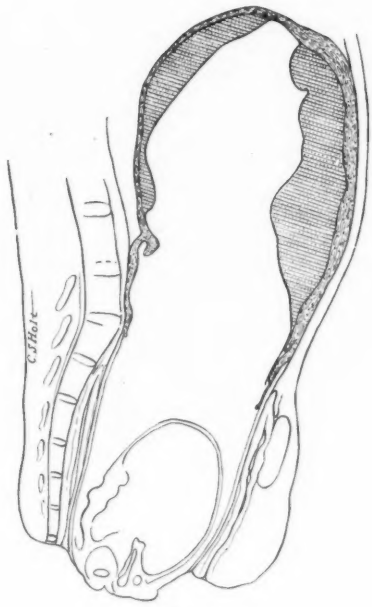

Fig. 7a.

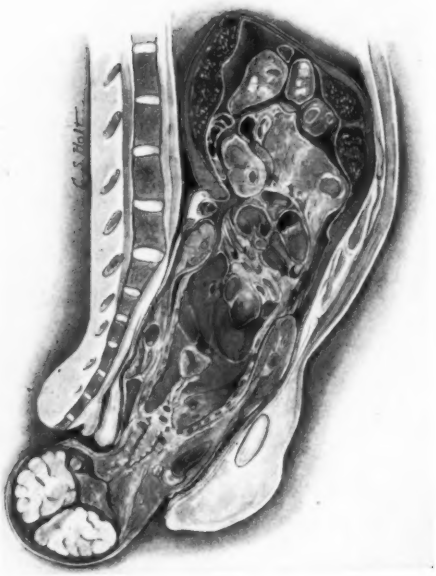

Fig. 8.

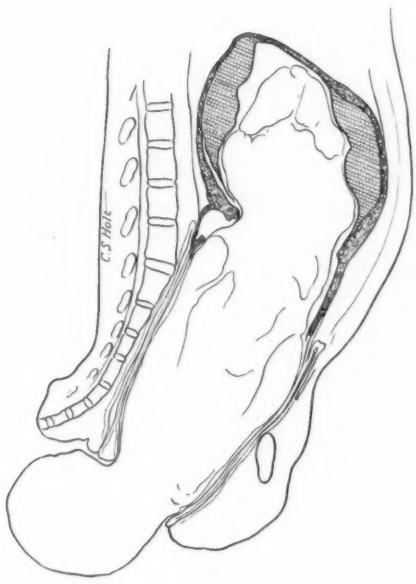

Fig. 8a.

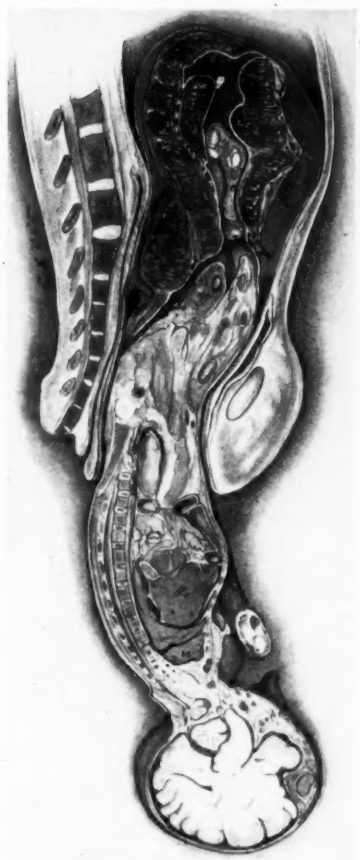

Fig. 9.

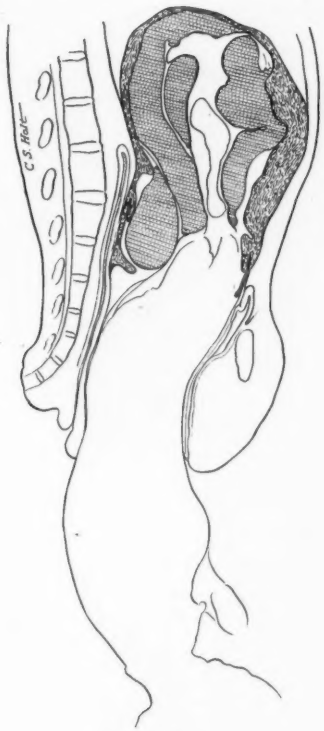

Fig. 9a.

because of its extreme variability in different specimens, and of the fact that in the second stage of labor the reflection is often found below the level of the external lip of the cervix. In the monkey, however, the question of differentiation of the three portions of the uterus is simplified by the presence of two more or less constant points. The first of these, the internal lips of the cervix, makes it possible in all specimens to distinguish precisely the lower extremity of the isthmus uteri. The second is not so constant, but in most specimens is an extremely valuable landmark. The placenta in the monkey is of the bidiscoidal type, the two discs being inserted one anteriorly and one posteriorly in almost all instances, and connected by large blood vessels which lie against one of the lateral walls of the uterus. Because of the regularity in extent of the placentae, and because of the rather obvious but unproved function of the anatomical internal os of limiting the lower extent of placentation, we have arbitrarily

TABLE V.—THE PER CENT OF REDUCTION IN TOTAL INTERNAL CIRCUMFERENCE IN VARIOUS STAGES OF LABOR

Stages of labor	E.O. to E.O.	Reduction cm.	Reduction %
Before labor	36.4		
I	43.3		
II A	34.9	8.4	19.4
II B	30.1	13.2	30.5
II C	26.1	17.2	39.7
III	18.5	24.8	57.2
P.P. 1 hr.–3 da.	18.1	25.2	58.2
P. P. 1 wk.	15.0	28.3	65.3

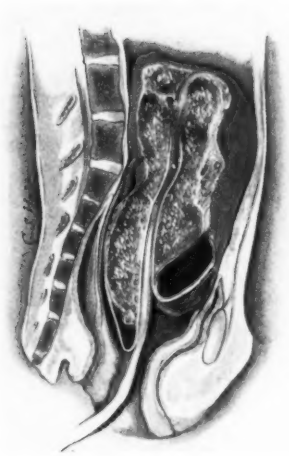

Fig. 10.

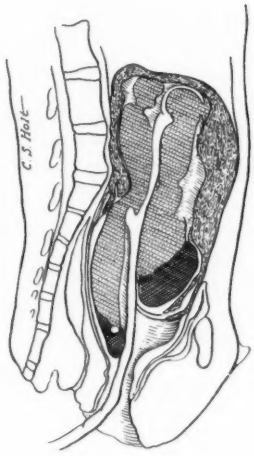

Fig. 10a.

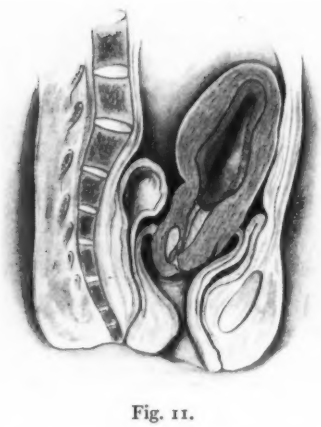

Fig. 11.

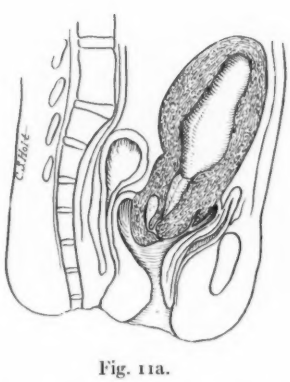

Fig. 11a.

chosen the lower border of the placenta as being at the approximate lower level of the corpus uteri. In addition to this, in many of the specimens the uterine wall thickens abruptly from below upward at a level coinciding with the lower border of the placenta. This finding adds credence to the arbitrary division indicated above. The authors realize fully that this is by no means a precise indication of the upper boundary of the isthmus. Because of the constancy of the findings, however, it appears that this is a satisfactory means of indicating the activity of this portion of the uterus, in contradistinction to the activity of the corporeal segment and cervix. In full cognizance, then, of the possible fallibility of the indicated upper extent of the isthmus uteri, we shall refer to the *isthmic segment* of the uterus as being that portion which lies between the internal lips of the cervix below, and (1) the lower border of the placenta or (2) the region of a physiological retraction ring, above. By these means of division of the uterus one may follow in successive specimens the activity of the *corporeal segment*, the *isthmic segment*, and the *cervix*.

This means of differentiation is well shown in Figure 13, which represents the internal

TABLE VI.—THE PER CENT RETRACTION OF THE UPPER AND LOWER UTERINE SEGMENTS IN RELATION TO THE ORIGINAL INTERNAL CIRCUMFERENCE OF THE UTERUS AND TO THE ORIGINAL LENGTH OF THE SEGMENT IN QUESTION (FROM O.I.O. TO O.I.O.)

Stage	No. of cases	Circumference cm. O.I.O. to O.I.O. with lips A	Circumference placenta to O.I.O. (L.U.S.) B	Circumference U.U.S. (A—B) C	% of internal circumference made up by L.U.S.	% of internal circumference made up by U.U.S.	% retraction L.U.S.	% retraction U.U.S.	% decrease in circumference due to retraction of	
									L.U.S.	U.U.S.
Before labor (term?)	3	35.0	10.7	24.3	30.6	69.4				
I	5	41.0	13.0	28.0	31.7	68.3				
II A	3	31.7	6.7	25.0	21.1	78.9	†48.4	†10.7	67.7	32.3
II B	7	27.4	5.2	22.2	19.0	81.0	60.0	21.0	57.0	43.0
II C	6	22.5	5.6*	16.9	24.9	75.1	57.0	40.0	40.0	60.0

L.U.S., lower uterine segment or "isthmic segment;" U.U.S., upper uterine segment or "corporeal segment."
*This increase is due to the failure of the L.U.S. of case 24 to retract.
†13.0 − 6.7 = 6.3 ÷ 13.0 = 48.4%.
28.0 − 25.0 = 3.0 ÷ 28.0 = 10.7%.
41.0 − 31.7 = 9.3; 13.0 − 6.7 = 6.3; 6.3 ÷ 9.3 = 67.7.

surface of the uterus of monkey 21. The fetus, membranes and placenta have been removed. The two lips of the cervix are apparent as ridges crossing the uterus at its extreme lower extremity and about 2 centimeters above this, respectively. The thickened "ring" above these ridges is the physiological retraction ring. The lower edge of the anterior placenta is seen to extend precisely to this ring, which marks the junction of lower and upper uterine segments. The posterior placenta was seen to have been placed somewhat laterally, but its lowermost extremity likewise reached just to this ring. In this specimen the maximum retraction of the isthmus posteriorly is readily evident.

In the consideration of results, the exact proportions of the term uterus prior to the onset of labor have not been estimated. The 3 animals which were sacrificed prior to labor were of smaller stature than the others of this series. In addition, the fetal proportions indicated that the animals were in late pregnancy, but not yet at term. The early first stage measurements are therefore taken as being representative of maximum term size of the uterus.

The results will be discussed under two general headings: (1) Changes in the uterus during labor, and (2) incidental pertinent observations. For the most part the results require but little discussion since the illustrations and tables are self-explanatory.

Changes in the uterus during labor. Stage I. During the first stage of labor there is only slight shortening in the total internal sagittal circumference of the uterus. The dimensions of the *cervix* and the position of the cervical lips with respect to the true conjugate are similarly not altered significantly—this despite

TABLE VII.—THE PER CENT OF THE TOTAL INTERNAL LONGITUDINAL CIRCUMFERENCE CONTRIBUTED BY THE CERVIX, ISTHMIC SEGMENT, AND CORPUS AT THE DIFFERENT STAGES

Stage	Isthmus cm. including internal lips A	Total external lips cm. B	Total internal lips cm. C	Circumference E.O. to E.O. without internal lips cm. D	Circumference O.I.O. to O.I.O. including internal lips E	Circumference O.I.O. to O.I.O. without lips (E—C) F	Isthmus without internal lips		Corpus		Cervix	
							cm. (A—C) G	%	cm. (F—G)	%	cm.	%
Before labor (term?)	10.7	3.6	2.2	36.4	35.0	32.8	8.5	23.5	24.3	67.1	3.6	9.9
I	13.0	4.1	2.0	43.3	41.0	39.0	11.0	25.5	28.0	65.0	4.1	9.5
II A	6.7	4.8	1.3	34.9	31.7	30.4	5.4	15.4	25.0	71.6	4.8	13.7
II B	5.2	4.1	1.1	30.1	27.4	26.3	4.1	13.2	22.2	73.7	4.1	13.2
II C	5.6	4.4	1.2	26.1	22.5	21.2	4.4	16.9	16.8	64.3	4.4	16.9
III	?	4.1	2.9	18.5	17.3	14.4					4.1	21.6

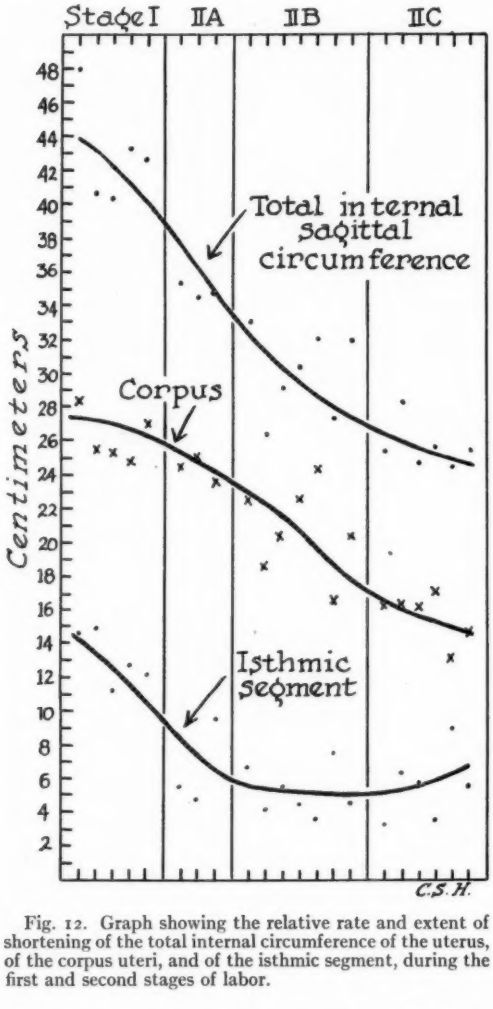

Fig. 12. Graph showing the relative rate and extent of shortening of the total internal circumference of the uterus, of the corpus uteri, and of the isthmic segment, during the first and second stages of labor.

the fact that dilatation is occurring. Estimations of *corporeal length* during the first stage show only questionably significant shortening. In contradistinction to the other portions of the uterus, *isthmic* shortening is definite and rather marked. These findings indicate, then, that during the first stage of labor retraction is more or less limited to the isthmus uteri (Fig. 12). Retraction or longitudinal shortening implies thickening. This observation is contrary to the usual conception of isthmic activity at this time in the human being. (In the calculations in the tables, the 100 per cent measurement of the first stage is taken as an average of all first stage animals, whereas individual animals during the first stage showed progressive, significant, isthmic shortening with no significant change in the corpus.

Stage II A. During the early part of the second stage isthmic retraction progresses, and at this time becomes maximal. Progressive shortening of the corpus is now evident. There is no appreciable change in the length of the cervix during this period. The change in the level of the cervical lips with respect to the true conjugate, however, is marked. It is seen that during this substage the anterior lip of the cervix rises above the level of the symphysis. The posterior lip also rises significantly, but not as extensively as the anterior.

Stage II B. Obviously just prior to the birth of a part much descent of the fetus has occurred, and this is reflected by an acceleration in the rate of corporeal retraction. Maximal shortening of the isthmic segment has already been attained, and is sustained throughout this substage. The length of the cervix itself has undergone little change, but the position of the lips with respect to the true conjugate shows further alteration. Anteriorly the external lip remains at a high level above the symphysis, and posteriorly the lip has reached the level of the sacral promontory.

Stage II C. Examination of the specimens in this substage shows that after a part is born the uterus contains but little of the fetus, most being found in the vagina, and that after half of the body of the fetus is born, the uterus contains only placenta and amniotic fluid. Hence, much shortening of the entire longitudinal circumference should and does occur. It is of especial interest that throughout the duration of labor the only evidence of longitudinal lengthening or mecystasis of the isthmic segment occurs when the placenta enters this segment. This is doubtless a type of receptive relaxation such as that manifested by the colon. Despite relaxation in the isthmus, the corpus continues to shorten as one should expect in order that evacuation of this portion of the uterus may be completed.

In the late second stage the upward excursion of the cervical lips is complete, the ante-

rior lip averaging almost 2 centimeters above the symphysis, the posterior being located at about the level of the sacral promontory. The extent to which the cervical lips rise in the monkey is greater than that revealed by the frozen sections in the human being and also greater than that seen in the experience of obstetricians. Since the upward excursion of the cervical lips is limited by the fascial supports of the cervix (which include the pubocervical fascia and the transverse cervical and sacrouterine ligaments), it is apparent that in the monkey these supports are more flexible than in the human being. Caldwell and Stillman of the Sloane Hospital for Women have made preliminary studies which clarify this subject in the parturient woman. Metal clips have been placed upon the cervix and x-ray pictures made during the various stages of labor. Their studies indicate that the cervical lips pull up considerably higher than is generally believed, but not as high as in the monkey.

Stage III. During the third stage there is continued shortening of the corporeal and isthmic segments. Cervical length, again, is not significantly altered. The almost instant return of the uterus to its general contour prior to the beginning of pregnancy is well illustrated by specimen No. 10, sacrificed one hour postpartum.

It has doubtless been observed that in this discussion of uterine changes during labor no mention has been made of the "thinning" which is believed to occur normally in the lower pole of the uterus. Our findings show that *longitudinal* thinning or actual stretching, does not occur normally in the isthmic segment in the monkey, with the single exception of the late second stage when the lower pole of the uterus relaxes to receive the placenta. All the evidence indicates that the region of the isthmus is not only the first portion of the uterus to undergo shortening in labor, but that, in addition, this shortening is progressive, and sustained until the late second stage. At cesarean section in the human being the illusion of thinning may possibly be produced by the contrast of the more marked and evident corporeal retraction, to the lesser but maximal retraction of the isthmus. Anesthesia may also be a factor. Actual longitudinal thinning of the isthmus may occur under certain circumstances in the human uterus, but we find no evidence of this in the monkey; nor have we found definite evidence of it in the human frozen sections in the absence of disproportion. In the instance of neglected disproportion the cervix is held fast by the taut cervical supports. Contractions of the powerful corpus uteri of necessity lead to longitudinal stretching with injury and ultimate rupture of the weaker lower pole of the uterus. The rupture of old cesarean section scars, often cited as evidence of isthmic thinning, occurs perhaps as frequently prior to, as during, labor. It is doubtless due to mecystasis or lengthening of the *circular* muscle, which occurs as the isthmus adapts itself to its contents during the second half of pregnancy, or as it enlarges laterally during early labor to allow the passage of the fetus.

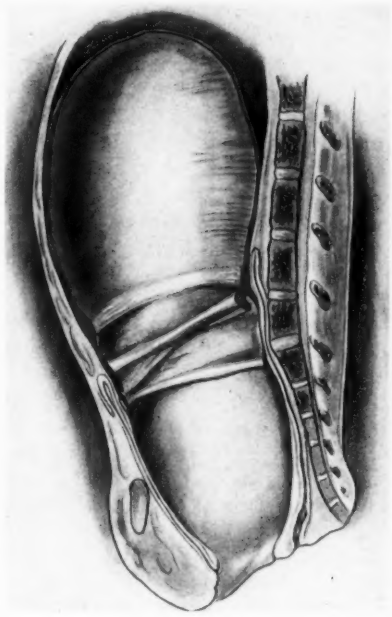

Fig. 13.

Incidental observations. The examination of the specimens brings to light many factors incidental to labor which heretofore have not been fully appreciated. Among these are:

Uneven retraction of the corporeal musculature. As may be observed in the illustrations, retraction is quite even throughout the corpus in the first and third stages, and fairly so in the early second stage. In the late second stage, however, retraction is grossly unequal in the various parts of this structure. Certain of the human frozen sections, notably many of those of Canton and Gonzalez, show similar inequality of corporeal thickness at this time.

Excursion, with ultimate complete obliteration, of the vaginal vaults. As the cervical lips rise in the pelvis, so must the vaginal fornices rise. This accordion-like action of the vagina is perhaps not fully appreciated. Its tremendous distensibility is well illustrated in Figures 9 and 9a.

Evidence of beginning separation of the placenta before completion of the second stage. If a monkey is unrestrained in the third stage of labor she will pull upon the umbilical cord immediately after the birth of the fetus, to remove the placenta. If it does not come away after the first pull, it generally does so after a few minutes. This indicates that in the monkey the placenta is almost completely separated at the end of the second stage of labor. This is verified by our sections. Early separation of the placenta has often been postulated in the human being, but there is no definite evidence either supporting or refuting it. In favor of such a postulation is the recent confirmation by Steer and Sullivan in a large series of cases that the placenta may be delivered almost invariably within 2 to 3 minutes after the baby, if a Credé maneuver is performed at the moment when the uterus first adapts itself to its suddenly diminished contents. This observation has been made by numerous other workers since its original presentation by Chantreuil in 1870, following the suggestion of Credé.

SUMMARY AND CONCLUSIONS

1. The present understanding of the anatomy of the nonpregnant and early-pregnant uterus has been outlined. The necessity of considering the isthmus uteri as an important and distinct part of the uterus has been emphasized. The terminology used is defined, and is based on anatomical, physiological, and on comparative anatomical and physiological observations.

2. Frozen sagittal sections of 30 Macacus rhesus monkeys at consecutive, chronological phases of late pregnancy, labor, and the puerperium have been made. Reproductions of 10 of these and of 1 of 3 nonpregnant animals are here presented. The entire series has been thoroughly studied with the view to determining the precise changes which occur in the laboring primate uterus. The conclusions recorded are based upon the analysis of the entire series of animals. All of the available human frozen sections have been similarly analyzed. The latter are not presented at this time. Although the human specimens were not satisfactory for the observation of many of the details, one receives the definite impression that the findings in the monkey are for the most part characteristic of those occurring in the human being, with only a few minor quantitative differences. Our observations concerning the changes in the human uterus are generally in agreement with the models prepared by Dickinson and Belskie, which are based upon a similar analysis of the human frozen sections.

3. In the *first stage of labor* retraction is limited chiefly to the isthmus uteri in the monkey. The intrinsic dimensions of the cervix do not alter appreciably despite the facts that dilatation occurs and that the lips rise to a slightly higher level in the pelvis. The total internal circumference of the uterus and the internal circumference of the corpus show only a slight amount of reduction in the first stage.

4. In the *second stage of labor* in the monkey the cervix rather quickly retracts to or above the true conjugate. Obviously, this elongates the vaginal portion of the birth canal. On the basis of the total internal circumference, retraction in the corpus and isthmus is at a proportionally similar rate during the early portion of the second stage. Maximal isthmic shortening occurs early, however, and is sustained until this segment relaxes to receive the placenta. The corpus, on the contrary, continues to manifest progressive shortening or brachystasis, which becomes especially marked after a part is born.

5. The cervical lips ascend to a higher level in the monkey than in the human being.

6. The question of "thinning out of the lower uterine segment" is discussed briefly. Longitudinal lengthening of the isthmic segment does not occur in the monkey, and human frozen sagittal sections do not support its occurrence in this species in the absence of disproportion. The isthmic segment does seem relatively thin in contrast to the corpus which lies above. The latter is more bulky to begin with, and it is possible that this may lead to the clinical impression of a "thinned out lower uterine segment," whereas, in reality, the isthmus is undergoing perceptible longitudinal shortening. Our material allows no conclusions concerning the activity of the circular muscle of the isthmus during labor. Obviously, however, definite circular lengthening of the lower pole of the uterus must occur in order that the fetus be allowed to pass. Circular lengthening, then, may account for thinning in the lower portion of the isthmic segment. However, this does not explain thinning as it is commonly thought to occur throughout this segment.

7. In the monkey, and likely in the human being, separation of the placenta is almost complete by the end of the second stage of labor. In our specimens the lower edges of the placenta were separated by the time a part was born, after which separation of the remainder of the placenta progressed rapidly.

8. At the beginning of the *third stage of labor* the uterus shortens and retracts still further. The placenta then lies partially in the vagina, partially in the lower pole of the uterus. After removal of the placenta there is almost instant return of the uterus to its general shape prior to pregnancy.

9. Some incidental observations are recorded.

The authors wish to express their appreciation to Miss Charlotte Holt for her interest in the preparation of the illustrations which accompany this presentation.

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RECURRENT FRACTURE

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IT is commonly believed that when a fracture heals without deformity the bone structure at the fracture site is as firm if not more so than before. This certainly seems to be true in most instances. Fractures which recur at the site of a fracture deformity or of an old pathological process where there is structural weakness are easily understood and do not call for comment. Such recurrent fractures were apparently frequent in the time before Roentgen and Lister when wound infection and the inaccurate reduction of fracture deformities were more common. There is, however, a group of cases deserving consideration in which the cause of refracture is not as apparent.

Small groups of these cases have received comment in the European literature. Troell, in 1917, reported 4 cases and mentioned a few others. He pointed out that the new fracture is never an anatomical copy of the old one, even when the latter is not completely healed. Disease, atrophy, and foreign bodies at the fracture site were thought to predispose to refracture. His cases included (1) a 50 year old man with a fracture of the humeral shaft, showing complete healing after operative reduction and then a refracture 5 months later; (2) fractures of the mid radius and ulna in a 12 year old patient, reduced by open operation and ivory implants, and a refracture 17 months later; (3) 2 fractures of the femoral neck occurring 6 years apart in a 65 year old male; and (4) 3 fractures of the tibia, the third one occurring 13 years after the other two, in a 31 year old male.

Peritz, in 1927, reported 6 cases in children between 9 and 16 years of age, 2 of whom were siblings. The children were otherwise healthy and there had been no other fractures. The interval between the fractures was from 5 weeks to 3½ months. As a possible explanation she gave deficient callus production at the first fracture site due to the very limited injury to the periosteum. Two of the fractures were subperiosteal in type, and there was formation of calcium-poor zones, such as are seen in hunger osteopathy and the so called "chronic" fracture. Other factors considered were late results of starvation during the war and an avitaminosis of the winter months, inasmuch as the cases appeared at that season of the year. It was further noted that all fractures had occurred in the mid-diaphysis and it was believed that an injury to the nutrient artery and the resultant changes in the bone might be a basis for refracture.

Strauss and Mandel, in 1932, reported 7 patients with fractures recurring after intervals of 4, 7, 13, 16, 28, 32, and 36 weeks. The patients were between 6 and 27 years of age; 3—14, 17 and 6 years of age—had fractures in the forearm, 3 in the lower leg, and 1 in the thigh. Although the fractures recurred at the exact sites of the old fractures, they pointed out the slightly different character and configuration of the fracture lines. They regarded refractures of this type as very rare and considered malnutrition as a factor in their causation.

Slaviero, in 1939, has reported 16 cases of refracture but most of these occurred in cases in which there was much deformity at the first fracture site or in which the first fracture had been complicated by infection. In 6 instances, however, the basis for refracture was not so readily apparent. These patients were 13, 12, 11, 16, 13, and 32 years of age, and the fractures had recurred after intervals of 8, 11, 6, 5, 21, and 22 weeks, respectively.

The x-ray was used very sparingly and, in some of the cases, it would appear that the healing of the fracture had not been complete. The author gives the general causes of defective healing which are well known but has regarded fractures of the forearm in children as a special instance. Here the fractures may be subperiosteal with insufficient injury to the periosteum to cause callus formation or there may be injury to a nerve or nutrient artery as a possible basis for the refracture.

MATERIAL

In a study of refracture, one may first consider a group of cases in which there is some demonstrable and reasonable basis for the second fracture. We have encountered instances of generalized and local pathological conditions of bone which predisposed to refracture and one instance in which a fracture had recurred many years after the implantation of a foreign body in the successful repair of the first fracture.

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Multiple fractures are a well recognized feature of osteogenesis imperfecta, but perhaps less well recognized is the tendency for the fractures to recur at the same site in different bones. This is well illustrated in Case 1 in which there were multiple fractures of both femora and of the right tibia, the recurrent fractures appearing at, or near, the old fracture sites. This is in part due to the deformity with which healing occurred, resulting in a structural weakness which predisposed to a refracture at that point. In other instances, however, it would appear that the healing of the fracture had occurred with the formation of particularly fragile bone in that area and this seems to be borne out by the character of the recurrent fracture line.

Recurrent fractures in an area of pathological bone structure and at the site of a foreign body are readily understood and are well illustrated by Cases 2 and 3. Nevertheless, it is of interest to observe that although the healing of the first fracture in Case 2 was apparently quite normal, in reality an osteitis fibrosa had developed and was not discovered until the time of the second fracture. In Case 3 there was without doubt a fragility of the bone structure about the bone screw implants, but this was not evident from an examination of bone structure by x-ray either at the new fracture site or of the intact bone about the proximal screw. Not only had there been no absorption of bone about the screws, but the bone was unusually dense.

The largest group of cases in this series is made up of those having recurrent fractures of the bones of the forearm. Others have commented on the peculiar liability of fractures involving the shafts of the radius and ulna in children to recur, and this is borne out by the fact that we have encountered 8 such cases although this is not one of the most common sites of fracture either in children or adults. The most common fracture in children is at the lower end of the radial diaphysis, 1 to 2 centimeters proximal to the distal epiphyseal line. No instances of a refracture in this area were encountered, and it may be inferred that here healing takes place with the formation of a bone structure more solid than before. This idea receives some support from Cases 16 and 17, in which a Colles' type of fracture was followed after a short interval, in 1 instance only 3 months, by a second injury with fracture in the forearm. Although the type of injury seemed to be due to the same mechanical forces, the second fracture did not occur at the old fracture site which would have been the case if that were a *locus minoris resistentiae*, but rather in the shaft some distance proximal to the old fracture site.

The 8 cases with recurrent fractures in the midportion of the shafts of the radius and ulna give evidence that in children, at least, healing of fractures in this area may fail to restore the bone to its original strength. The altered character of the bone structure after healing is shown by the peculiar configuration of the second fracture lines which was observed in all instances and suggests an abnormal fragility of the bone. These second fracture lines resemble the fracture lines seen in osteogenesis imperfecta, as well as the fracture lines observed in rickets and the "insufficiency fracture" described by Hansson and others.

One reason that has been suggested for the increased fragility in these cases is an involvement of the nutrient foramen and a consequent impairment of the blood supply to the bone. This is conceivable in Cases 4, 6, 10, and 11, but would not apply to Cases 5, 7, 8, and 9, in which the fractures have occurred at some distance from the positions usually given for the nutrient foramen. Nevertheless, it is possible that in the shaft where the cortex and medulla are sharply differentiated, the blood vessels or nerves may be more seriously injured than in the cancellous portions without actual involvement of the foramen.

Other possibilities for the fragility of the bone are the complications present during healing in some of the cases: a pressure ulcer in the skin of Case 4, a respiratory infection and incomplete immobilization of the arm in Case 7, chickenpox in Case 9, and soft tissue atrophy in Case 10.

A further possibility is a constitutional peculiarity of these children. Many of them tended to be undernourished, and the extremities were strikingly thin and wiry. Six of the 8 were definitely below the average weight for their age and height and were described as "poor eaters" and "delicate," as compared with their brothers and sisters. A mild form of osteogenesis imperfecta is suggested by the thin bluish sclerae and the hyperflexibility of the ligaments which many showed.

In the treatment of fractures of the forearm in children, where the shafts of the radius and ulna are involved, it seems advisable to recommend that these children, and those responsible for their care, guard against the possibility of further injury even after recovery seems complete. The liability to refracture might also be lessened if the food intake could be increased and the nutritional state improved.

Comparable in many respects to the 8 cases of refracture in the radius and ulna are the 2 cases (12 and 13) of refracture in the clavicle. The

April 20, 1938. April 13, 1939. September 14, 1939. August 13, 1940.

Fig. 1. Case 1. Severe osteogenesis imperfecta with numerous fractures of the bones of both legs. Fractures occurred in the left femur in April, 1933; April, 1938; April, 1939; and August, 1940. All of these fractures took place at the same site in the femoral shaft after osseous union had occurred.

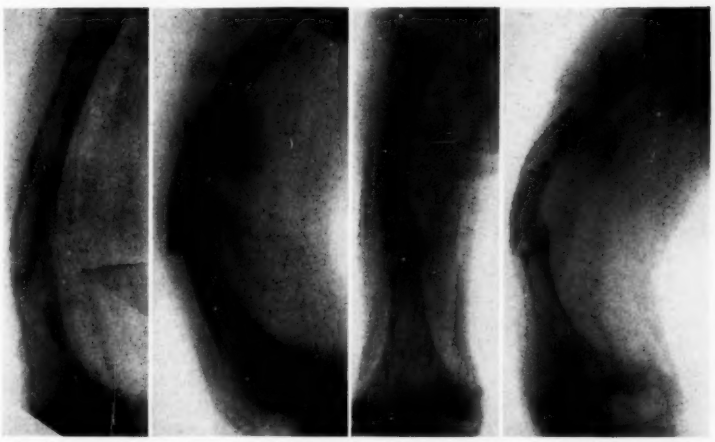
shafts were involved where the cortex and medulla are sharply differentiated and near the nutrient foramen. Both children suffered upper respiratory infections during the period of healing and the character of the second fracture lines indicated an abnormal fragility of the bone. Some features of osteogenesis imperfecta were observed in Case 12, and this patient was below the average weight for his height and age.

Two cases remain which present certain new features and raise new questions. Case 14 is not strictly pertinent to this study for, although the 2 fracture sites in the tibia appear identical, the growth of the bone during the interval of 6 years has displaced the old fracture site some distance distal to the new fracture site.[1] Thus we are not faced with a true exception to the observation that refractures occur in the compact structure of the shaft rather than in the spongy areas at the ends of the long bones. Case 15 concerns a very obese boy of 18 who sustained 3 fractures in the same area of the fifth metatarsal bone with intervals of 5½ months and 4½ months between them. The fractures were each preceded by a definite acute trauma producing severe pain and each injury was sustained in a slightly different way under different circumstances. March fractures usually involve the second metatarsal bone although Koch has described one in the fifth metatarsal in a deformed foot. Furthermore Watson-Jones states that metatarsal fractures due to muscle strain may recur. Although the obesity in this instance may have been productive of muscle and bone strain, an insidious history of progressive pain without acute injury which is characteristic of march foot is quite unlike the history in this case. The rather short interval between the fractures suggests that healing may not have been complete at the time of the refracture. This is contradicted, however, by the facts that the patient made a complete clinical recovery after each fracture, using his foot in a normal manner again without pain and that the new fracture lines were of slightly different configuration than the old ones.

[1] A study of the chart in a monograph of the Society for Research in Child Development (16) giving the growth in length of the tibial shaft during childhood indicates an average growth of 12 centimeters in the interval between the fractures. Assuming a growth of 6 centimeters at each end would bring the new fracture well proximal to the old fracture site. Inasmuch as the child was very close to the average weight and height and the growth of the tibia is about equal at each end, this assumption seems valid.

FURTHER FACTS ON RECURRENT FRACTURES

Upon the observation of a recurrent fracture, the question arises as to whether the healing of the first was complete. In some of the cases the x-ray studies indicated complete healing and in all cases there was clinical evidence of healing



April 20, 1938. August 29, 1938. November 29, 1938. September 14, 1939.

Fig. 2. Case 1. Similar changes are seen in the right thigh where fractures of the femur are known to have occurred in June, 1937; April, 1938; August, 1938; and (?) September, 1939.

as indicated by normal use of the part without pain. The interval between the fractures, although in some instances barely over 3 months, exceeded the period generally considered necessary for healing in uncomplicated cases. However, the available clinical evidence of complete healing of human fractures is admittedly not entirely adequate and for further information one must turn to animal experimentation. Lindsay and Howes, in 1931, reported studies on the breaking strength of healing fractures in the fibulas of rats. They quote Leriche to the effect that the healing rate in bone was the same for all animals that he studied so that their results may have an applicability to man. They found the breaking point of the rat fibula to be at a strain of from 285 to 580 grams. During healing, strength first appeared at the fracture site on the sixth day and there was a rise in strength to an average resistance of 341 grams at 21 days. This was followed by a slight fall to 277 grams on the thirty-third day and a subsequent rise to 465 grams at 45 days. At this time the bone at the fracture site was as firm as elsewhere and there was no predilection for the fracture to occur at the old fracture site. The first peak of healing strength coincided with the maximum extent and density of the callus and the subsequent fall was correlated with the absorption of the callus surrounding the bone and in the medullary canal. Further observations (6-9) with the rats on various diets showed most consistently that "changes in the quantity of food consumed and the rats' weight exert a strong influence on both the healing and the normal breaking strength of the fibulas." The greatest loss of strength was noted on a high carbohydrate diet with lesser changes on a high fat, low calcium diet. Maximum healing strength was obtained in about 45 days on all diets.

November 29, 1938. Sept. 14, 1939. December 18, 1939.

Fig. 3. Case 1. The right lower leg with fractures of the tibia in November, 1938; September, 1939; and December, 1939.

December 7, 1938. March 28, 1939. July 19, 1939.

Fig. 4. Case 2. Two recurrent fractures in the shaft of the right tibia in a French-Canadian boy who sustained the original fracture on November 25, 1933, at the age of 3 years and 7 months. The original films are not available but the report indicates no abnormality in the bone structure at the fracture site at that time. The healing was apparently satisfactory although a cystic formation was discovered at the time of the second fracture on December 7, 1938. A third fracture occurred on July 19, 1939, and this was followed by surgical exploration with a diagnosis of osteitis fibrosa cystica on the material removed for pathological study.

August 28, 1934. September 13, 1934. August 11, 1939.

Fig. 5. Case 3. Recurrent fracture of the femoral shaft in an 8 year old boy 5 years after the original fracture which was treated by open operation and the implantation of two bone screws.

Haebler and Reiss, in 1936, made studies on the tension and bending strength of excised canine long bones. No relation could be established between the flexibility to bending or tension and the age, weight, length, or in the calcium or water content of the bone. This is admittedly in contrast to man in whom the fragility of bones in the aged and the flexibility of the bones in the child are well recognized. Marked differences were found in different bones of the same animal. In studies on healing fractures they found that the extent and density of the callus as demonstrated by x-ray may be misleading in estimating the strength at the fracture site, and there was no close correlation between the calcium content of the dried material at the fracture site and the firmness of healing. Water content seemed to be of considerable importance. They believed the best evidence of healing to be painlessness under strain.

The effect of the diet and vitamin intake on the healing of fractures has been subject to much study. A review of this material was published in a monograph by Hertz, in 1936. Recurrent fractures during attacks of scurvy were reported in sailors by Richard Walter in 1749, Mead in 1762, Marriques in 1783, Bell in 1788, Callisen in 1798, Hammick in 1830, Budd in 1840, and Moore in 1859. Israel and Fraenkel studied this phenomenon experimentally and found that scurvy may soften a callus already formed and facilitate refracture. Their findings were supported by the experiments of Schilowzew and contradicted by those of Roegholt. Hertz made experiments on scorbutic guinea pigs and could not substantiate the conclusions of Israel and Fraenkel. Thirteen animals with fractures of the fibula were placed on a scorbutic diet after 28 days, and they died in from 54 to 71 days. All of the fractures were found well healed. Hunger osteopathy and the occurrence of a chronic fracture as the result of mechanical strain are offered as an explanation for the observations in scorbutic sailors and in the animals studied by Israel and Fraenkel. Delayed healing of fractures in subjects deficient in vitamins A, B, and D has been reported. In the cases of recurrent fracture which we have studied there was no evidence of vitamin deficiency either in the history of food intake or in the appearance of the bone structure. However, an impressive number of the patients were underweight and had a poor appetite so that possibility of some food deficiency and dietary osteopathy must be considered.

A number of papers have appeared, chiefly in the foreign literature, on the occurrence of in-

sidious or chronic fracture. The best examples are the march foot and the fissure fracture of the tibia which are prone to occur in young military recruits subjected to unaccustomed strain. Cases have been described and discussed by Koch, Ollonquist, Reischauer, Hansson, Pfahler, and others. It is generally agreed that there is no acute trauma, but that under the influence of prolonged strain a periosteal proliferation occurs followed by the appearance of a fissure in the cortex. The symptoms are insidious in onset and progressive in character. The first x-ray studies may be negative as the callus does not become demonstrable for 8 weeks or more (Koch). Fractures of this type also are seen in undernourished individuals as a manifestation of a hunger osteopathy or rickets. Although the fracture lines bear a certain resemblance to the refractures seen in this study, an identity cannot be established, for in all of our cases the refracture was accompanied by a very definite history of acute trauma, and there was no deformity or habit of behavior productive of a chronic strain. Furthermore, the old fractures were symptomless at the time of the refracture.

CONCLUSIONS

1. Fractures are prone to recur when a general or local disease of the bone is present, when healing has occurred with deformity, and at the site of a foreign body. The basis for such fractures is readily understandable.

2. A fracture may also recur at an old fracture site after healing has apparently been complete and in the absence of a significant deformity or recognizable complicating pathological process.

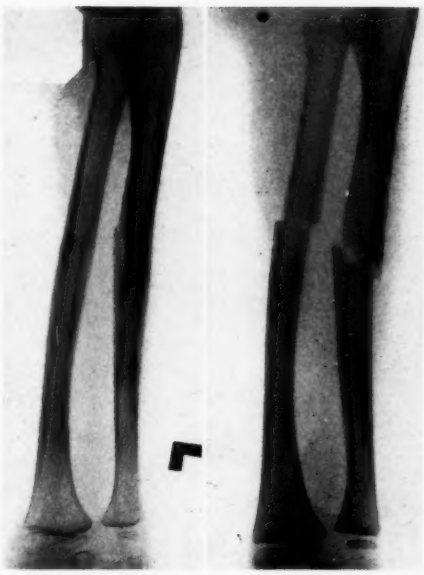
3. The character of the new fracture indicates an abnormal fragility of bone at old fracture site.

4. Recurrent fractures of this type are most often seen in the shafts of the radius and ulna of children. Such children are apt to have poor appetites and to be of less than average weight with thin extremities. The flexible ligaments and blue sclerae which many of them show suggest a constitutional background in common with osteogenesis imperfecta.

5. It seems desirable for children who have had fractures of the shafts of the radius and ulna to take particular care against a second injury even after the healing of the first injury appears complete and to increase their food intake for the improvement of their nutritional state.

CASE REPORTS

CASE 1. M. S., C. H. D 3140. A white female of English nationality born on March 15, 1932, was first seen at the Children's Hospital in April, 1938, having recently sustained a spontaneous fracture of the left femur. The dates of previous and subsequent fractures are as follows: the left femur in April, 1933, April, 1938, April, 1939, and August, 1940; the right femur in June, 1937, April, 1938, August, 1938 and (?) September, 1939; the right tibia in November, 1938, September, 1939, and December, 1939.



September 5, 1939. August 12, 1940.

Fig. 6. Case 4. Recurrent fractures of the left radius and ulna in a 9 year old boy after interval of 1 year and 1 month. First view shows appearance of healing at fracture sites 6 weeks after the first injury. Healing was complicated by a pressure sore but recovery was eventually complete. Second view showing new fractures of different character at the old fracture sites.

On May 28, 1938, the neck was explored surgically and a parathyroid gland somewhat larger than usual, encountered at the right lower pole of the thyroid gland, was removed. Microscopic study of the specimen revealed nothing remarkable and the operation had no demonstrable effect on the patient's course. Theelin was given for a period without effect. An x-ray study of the spine in September, 1939, showed a low mineral content of the bone structure, and the vertebral bodies had a marked biconcave configuration as the result of expansion of the intervertebral discs. Multiple fractures of the ribs were also noted. The fractures of the left femur are illustrated in Figure 1 and show the tendency to recurrence in the areas of abnormal bone structure at the old fracture sites. The condition has been regarded as an osteogenesis imperfecta and except for the deformities incident to that, the physical examinations have not been remarkable.

CASE 2. R. P., C. H. 92720. This boy, born of French-Canadian parentage on April 25, 1930, was first seen at the Children's Hospital in 1932 for bronchoscopic removal of a peanut. He was next seen on December 7, 1938, giving a history of falling while chasing another boy and injuring his right leg. It was later learned that a fracture had

November 26, 1939. March 26, 1940. April 29, 1940. June 18, 1940.

Fig. 7. Case 5. Recurrent fractures of the right radius and ulna in a 7 year old boy after an interval of 5 months. The first two views show the first fractures with the appearance of satisfactory healing after 4 months. The second fractures are at the old fracture sites but are of different character.

occurred in the right tibia 5 years previously, followed by satisfactory healing.[1] X-ray studies here in 1938 (Fig. 4) showed an oblique fracture through an area of cystic disease in the middle third of the tibial shaft. There was no deformity as a result of the fracture and a cast was applied for 7 weeks. Healing occurred and the normal use of the part was regained although the area of pathologic bone structure persisted.

On July 19, 1939, he fell again, sustaining another fracture in the right tibia with fracture lines similar but not identical to those observed previously. Healing was again occurring but it was decided to curette the cystic area and fill the cavity with bone chips. This was carried out on October 4, 1939, and pathological study of the material removed showed the characteristic appearance of osteitis fibrosa cystica. Satisfactory healing occurred with an uneventful recovery and subsequent roentgen-ray studies on October 31, 1939, December 26, 1939, March 12, 1940, and May 14, 1940, and November 12, 1940, revealed increasing solidity of the bone structure with no new areas of cyst formation.

Case 3. J. S., C. H. 117461. This patient, of French-Syrian parentage, born on July 16, 1931, was struck by a truck which passed over his left leg on August 7, 1934. A comminuted fracture of the lower tibia was recognized and treated accordingly. On August 28, 1934, a deformity of the left thigh was noted and a long oblique fracture of the femoral shaft was discovered (Fig. 5). The fragments were overriding about 3.5 centimeters, and there was callus at the fracture site, giving an appearance compatible with the date of the first injury. Because of the deformity an open reduction was performed with removal of the callus, resection of the sclerotic ends of the fragments, traction, and correction of the overriding. With the fragments in close end-to-end approximation two bone screws were inserted. A plaster cast was applied for 8 weeks, at the end of which time "good union" was reported.

There was no disability or complaint until August 10, 1939, when he jumped about 10 feet from the roof of a garage and experienced pain and weakness in the left leg. X-ray studies showed that there had been complete healing at the old fracture site in the femur with no demonstrable osseous change about the bone screws. However, a new fracture had occurred involving the site of the more distal screw with a somewhat different configuration and character of the fracture line. After unsuccessful attempts at manipulation, an operation was performed on August 26, 1939, and the lower screw, which lay between the fragments, was removed. The upper screw was firmly in place and could not be moved. Two steel Parham bands were applied with the fragments in close end-to-end approximation. Healing occurred rather slowly and on April 12, 1940, he was allowed up on crutches with a caliper brace. On October 8, 1940, the brace was removed and there was no pain or disability in walking except for a very slight limp.

At an interview on November 2, 1940, the patient was observed to be an active, well nourished, and well developed boy weighing 33.5 kilograms for a height of 137 centi-

[1]The x-ray report from another hospital dated November 25, 1933 describes an oblique fracture of the middle third of the right tibia. No mention is made of any cystic formation.

meters. There had been no other fractures than those here described, and in a family of 5 other siblings only one fracture had occurred and that was sustained in an auto accident. The diet had been adequate and well balanced. The sclerae appeared bluish but there was no deafness or abnormal flexibility of the ligaments.

CASE 4. S. A., C. H. C 2530. This Armenian boy, born on March 2, 1931, fell while climbing the back of a chair and injured his right arm, in April, 1937. The x-ray studies revealed greenstick fractures of the midradius and ulna. Following manipulation and immobilization satisfactory healing occurred without deformity or disability.

On July 22, 1939, in a fight over a toy wagon, he was attacked by another boy and the two fell to the ground on his outstretched left arm. X-ray studies made in Providence, Rhode Island, showed fractures of the middle thirds of the left radius and ulna with lateral and anterior angulation at the fracture sites. The deformities were reduced, and a fixation dressing was applied. On August 7 a large pressure sore was discovered and a new dressing was applied. On his return to Detroit, x-ray studies were made at the Children's Hospital on September 5, 1939 (Fig. 6), and the fracture sites are well shown with bony union occurring in a satisfactory manner. The child recovered the use of his arm completely.

Enlarged tonsils were removed on April 22, 1940, and at that time the physical examination was otherwise negative.

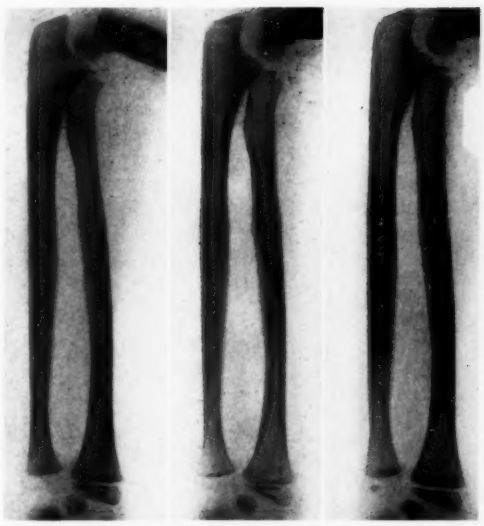
In August, 1940, while boxing he was tripped by his opponent and fell backward on his extended left wrist. X-ray studies on August 12, 1940 (Fig. 6), showed new fractures in the middle thirds of the left radius and ulna. It was evident that complete healing had occurred at the old fracture sites and the new fractures, although occurring in the same area, had a slightly different configuration of the fracture lines. Following manipulation, healing again took place.

The boy appeared quite thin and very active, weighing about 24 kilograms with a height of 131 centimeters. This is a constitutional type shown by his parents and a sister. He was described as a "poor eater" but with no peculiarities of taste and with a good vitamin intake. No fractures other than those described have been sustained by him or his family. The sclerae were rather thin but not definitely blue. There was no deafness. The ligaments about the joints were quite flexible but not abnormally so.

CASE 5. W. S., C. H. 118080. A male child, born January 15, 1933, of German extraction, was first seen at the Children's Hospital in November, 1936, when a tonsillectomy was performed for large tonsils. The physical examination was otherwise negative. On November 26, 1939, he was pushed from a porch by his brother and sustained fractures of the right radius and ulna (Fig. 7). The deformity was reduced by manipulation, and immobilization in plaster was carried out for 10 weeks. Frequent x-ray examinations revealed satisfactory progress in healing, and on March 26, 1940, healing was thought to be complete. The clinical findings confirmed this, and the boy made free use of his arm without complaint.

On April 28, 1940, 5 months after the previous injury and 2½ months after free use of the arm was allowed, he sustained a new injury to the right forearm in a fall while jumping during a game. The x-ray examinations revealed new fractures of the radius and ulna at the old fracture sites. There was, however, a slightly different configuration of the fracture lines. Immobilization in plaster for 7 weeks resulted in satisfactory healing at both fracture sites.

At an interview on October 16, 1940, the x-ray examination showed complete healing with minimal deformity, and there was free use of the arm without discomfort. He appeared to be a rather thin and very active boy, weighing 27 kilograms with a height of 129 centimeters. He had suffered no fractures other than those described but gave evidence of many minor cuts and bruises. There was no deafness but the sclerae were slightly bluish and the ligaments were of somewhat more than average flexibility.



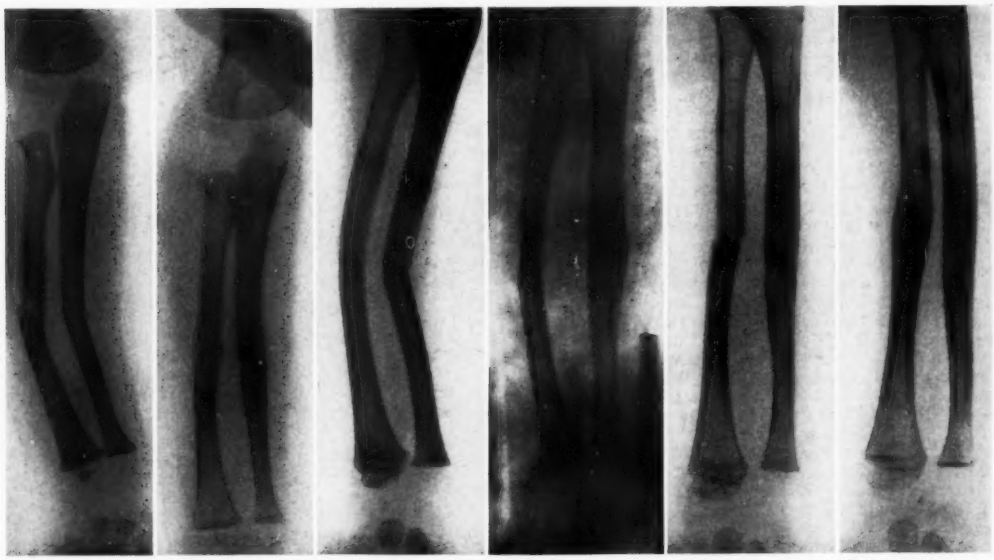
February 23, 1940. March 11, 1940. June 27, 1940.

Fig. 8. Case 6. Recurrent fractures of the right radius and ulna in a poorly nourished, 7 year old girl, after an interval of 4 months and 2 weeks. Healing of the first fractures seemed satisfactory clinically and by x-ray on March 11, 1940, 2½ weeks after the injury. The second fractures are distinctly different in character and delineation although occurring at the old fracture sites.

CASE 6. L. D., C. H. 105617. A girl of Irish parentage, born on December 12, 1932, was first seen in the Out Patient Department in 1934, with eczema. She complained of a prolonged cold with cough in 1939 and much enlarged tonsils were found. The tuberculin skin test was negative.

On February 16, 1940, her right arm was pulled violently while playing with an older girl, and an x-ray examination 1 week later revealed transverse fractures of the middle thirds of the radius and ulna, the only deformity being a slight anterior angulation at the fracture sites. Immobilization in plaster was carried out for 6 weeks, and there was the usual progress in healing observed clinically and by x-ray. At the end of 6 weeks she was allowed free use of the arm and, although writing with the right hand, she continued to use the left for eating and striking other children.

The second injury occurred on June 27, 1940, in a fall from a bicycle, and new fractures of the right radius and ulna were observed at the old fracture sites with, however, a slightly different character and configuration of the fracture lines. Following manipulation the right extremity was placed in immobilization in plaster for 9 weeks and there was again satisfactory progress in healing of the bone at the fracture sites.



November 11, 1935. February 24, 1936. January 11, 1939. March 21, 1939. August 24, 1939. October 17, 1939.

Fig. 9. Case 7. Left forearm of a male child who sustained fractures of the radius and ulna on 4 occasions—November 10, 1935; December 29, 1935, January 10, 1939; and August 24, 1939. On the first occasion healing was complicated by an upper respiratory infection and incomplete immobilization. There was good functional recovery and no deformity following the second, third, and fourth injuries.

September 4, 1937. November 4, 1939. December 3, 1940. December 28, 1940.

Fig. 10. Case 8. Recurrent fracture of the left radius in a poorly nourished 10 year old girl after an interval of 3 years and 3 months. At the first injury both the radius and ulna were involved and healing was observed to be complete 2 years later on November 4, 1939. The second fracture of the radius occurring at the injury of November 22, 1940, was inconspicuous in the study of December 3, 1940, but is confirmed by the appearance of callus on December 28, 1940.

The patient was interviewed on October 16, 1940. There was free use of the arm without deformity or disability and the x-ray examination revealed complete healing at the fracture sites. She was observed to be an unusually small and thin, but very active girl, weighing 18.5 kilograms with a height of 120 centimeters. This was a constitutional trait shared by the mother and her other children. She had suffered no fractures other than those described and only

November 20, 1940. November 20, 1940. March 1, 1941.

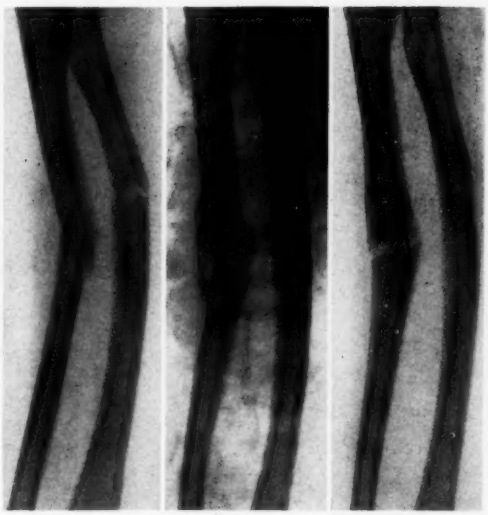
Fig. 11. Case 9. Recurrent fractures of the right radius and ulna in a 7 year old girl after an interval of 3 months and 1 week. Healing of the first fracture was complicated by chicken pox but appeared complete with no deformity or disability. The second fractures, although at the old fracture sites, have a different course and character.

one other fracture in the family was recalled. She had been examined recently in the medical clinic, but no cause for her low weight was discovered. Her mother described her as a poor eater but there were no fancies or peculiarities of the diet. There was no deafness but the sclerae were thin and slightly bluish and there was more than usual flexibility at the joints.

CASE 7. M. S., C. H. E 286. This boy, born of Irish parentage on December 14, 1933, was seen at another hospital on November 11, 1935, the day following a fall out of bed and an injury to his left arm. The x-ray studies (Fig. 9) disclosed fractures of the midradial and ulnar shafts. Further study after the application of a plaster dressing showed an excellent end-to-end approximation of the fragments and a good alinement except for slight posterior angulation at the radial fracture site. The records do not reveal the length of the period of immobilization, but there is a note that on December 7, 1935, the cast was cut and passive motion applied. Convalescence was prolonged and complicated by an upper respiratory tract infection without elevation of temperature and with a negative x-ray study of the chest on December 10, 1935, and he was not discharged from the hospital until December 22, 1935.

Six days later he fell while playing and again injured the left arm. X-ray films showed new fracture lines at the old fracture sites and a rather marked degree of posterior angulation. Following manipulation and immobilization an excellent position and alinement of the fragments was observed at the roentgen studies of December 29, 1935, January 25, 1936, and February 24, 1936.

Recovery was apparently complete and he had normal use of his arm until January 10, 1939, when he was pushed from a bed while playing with his sister and sustained a new injury to the left arm. Fractures were again seen in the radius and ulna at the old fracture sites. The disalinement was corrected and immobilization in plaster was maintained for 10 weeks. Good use of the arm was regained and the clinical impression on April 18, 1939, was that the fracture was completely healed. On June 12, 1939, his foot became caught in a bicycle. Pain persisted and an x-ray examination on June 15, 1939, revealed a greenstick fracture at the lower end of the tibia. Immobilization in plaster was carried out for 6 weeks and satisfactory healing occurred.



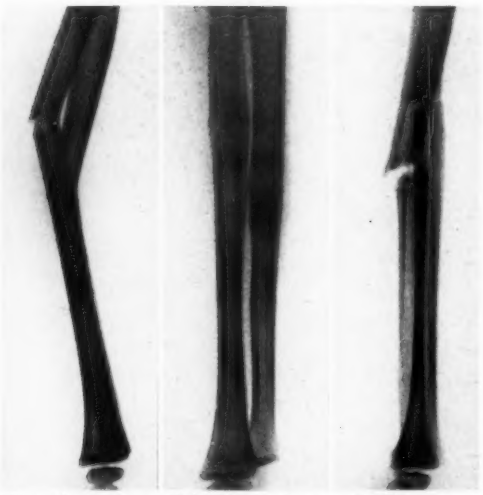
June 27, 1940. August 22, 1940. February 9, 1941.

Fig. 12. Case 10. Recurrent fractures of the left radius and ulna in a 14 year old girl after an interval of 7 months and 2 weeks. Healing of the first fractures was complicated by considerable atrophy, but there was no other deformity and good function was obtained. The second fracture lines are of distinctly different character than the first, although occurring at the same sites.

On August 24, 1939, he sustained a fourth injury to his left arm when pushed by some boys at play and for the fourth time a fracture was demonstrated in the midradius. The ulna appeared intact at this time. Satisfactory healing occurred with immobilization in plaster for 9 weeks.

At an interview on October 16, 1940, the boy was observed to be very active physically and mentally. He weighed 22.5 kilograms with a height of 117 centimeters and appeared well nourished. His mother had observed that in the past his wrists had appeared thin compared with those of his brothers and sisters and he had inclined to be "delicate" although he had recently become more robust. His diet seemed satisfactory and he had a good appetite, but he had small, poorly developed teeth. The sclerae appeared bluish and the ligaments were quite flexible at the joints but there was no deafness. He had sustained no fractures other than those described. One sister had suffered a fracture of the clavicle in an accident but no other fractures in the family were recalled.

CASE 8. R. O'C., C. H. C 4098. This girl, born of Irish parentage on October 24, 1930, was first seen at the Children's Hospital on June 14, 1937. She had large tonsils and an uneventful tonsillectomy was performed on July 18, 1937. On September 3, 1937, she fell about a foot while playing on a small tree stump, injuring the left arm and crying with pain for 2 hours. The x-ray examination the



December 1, 1940. February 4, 1941. April 8, 1941.

Fig. 13. Case 11. Recurrent fractures of the left radius and ulna occurring in a 9 year old boy after an interval of 4 months and 1 week. The healing of the first fractures was complete by x-ray films February 4, 1941, and by clinical examination, and free use of the part was regained. The different character of the new fracture lines at the old fracture sites is well shown.

next day showed transverse greenstick fractures in the middle thirds of the radial and ulnar shafts with slight palmar angulation at the fracture sites. After the manipulation a plaster dressing was applied for 6 weeks. Satisfactory use of the part was obtained but for some time there was tenderness about the fracture sites and for a long time the part would ache during inclement weather. Even when recovery seemed complete her mother noted that she would tend to protect that arm. A second injury occurred on November 4, 1939, when she was struck in the posterior aspect of the lower part of the left upper arm. Swelling and ecchymosis appeared, and there was pain for a few days but the x-ray studies were negative and there was observed to be a normal appearance of the bone structure at the old fracture sites, with no deformity. The arm was carried in a sling for 3 weeks, and a good recovery was obtained.

On November 22, 1940, she fell 12 or 14 feet while playing on the edge of a sand pit, again injuring the left forearm, and there was immediate severe pain causing her to cry for 2 hours. The pain persisted and on December 3, 1940, she came to the clinic for x-ray studies. These showed a soft periosteal shadow about the middle third of the radial shaft at the old fracture site and a very slight disturbance in the bone structure which was not present at the examination of November 6, 1939. Re-examination on December 28, 1940, showed some resolution and increased density of the periosteal deposits and the irregularity of the bone structure was seen a little more clearly so that there was no reasonable doubt that a second fracture of a very limited subperiosteal type had occurred at the old fracture site.

At the interview of December 28, 1940, there was no complaint of pain and she exhibited free use of the arm, although her mother said that there was sometimes pain at night requiring a hot water bottle. She had sustained no other fractures nor were there fractures in any of 6 siblings. Her appetite had been generally poor and she cared little for meat or vegetables. She was decidedly thinner and less robust than her healthy brothers and sisters. Her weight at this time was 26 kilograms for a height of 138 centimeters. The ligaments about the joints showed more than the usual flexibility and the sclerae appeared thin with a bluish cast. There was no deafness.

Case 9. N. McK. A white girl born on March 25, 1933, and living in comfortable circumstances, tripped over her rubbers while running on a playground at school and fell on her extended right arm on November 20, 1940. She was referred to us a few hours later as a private patient of Dr. Charles Kennedy and the x-ray examination disclosed greenstick fractures of the radius and ulna near the junction of their middle and distal thirds with a sharp anterior and medial angulation at the fracture sites. Under ether anesthesia the normal alinement was restored, and a plaster dressing was applied. Re-examination with the dressing *in situ* showed the fragments in close end-to-end approximation with an excellent alinement in both planes. The immobilization was maintained for 4 weeks and then was discontinued temporarily for early physiotherapeutic measures, extending over a period of 3 days, when the cast was discarded entirely. Convalescence was complicated at this point by an attack of chickenpox, but the normal use of the right arm was regained and there was no complaint or deformity of any kind.

On March 1, 1941, while roller skating she fell again on the right arm and sustained a marked deformity as before. Refractures at the old fracture sites were demonstrated on the x-ray films but with a slightly different character and configuration of the fracture lines. There was again marked angulation toward the radial and volar aspects.

At an interview on this date she was observed to be a fairly well nourished blond girl of pleasing appearance and weighing 27 kilograms with a height of 135 centimeters. The arms and legs were quite thin and there was more than the usual flexibility at the joints. Her mother described her as a "poor eater" taking food very slowly and having an aversion to meat. She liked a variety of vegetables, however, and drank three glasses of milk daily. The sclerae were white and there was no deafness. The patient had sustained no fractures other than those described and none had been experienced by her mother or 4 sisters. Her father has been involved in accidents with fractures of the nose and at the ankle.

Case 10. E. W. This girl, a private patient of Dr. Darling of Pontiac, Michigan, was born on June 8, 1926. On June 27, 1940, while playing out of doors she jumped on a bench which tipped over and she was thrown to the ground on her outstretched left arm. Fractures of both bones of the forearm occurred, the ulnar fracture being quite oblique, with the end of the proximal fragment perforating the skin. X-ray studies (Fig. 12) on the same day showed the fractures with angulation anteriorly and toward the radial side particularly at the ulnar fracture site.

The deformity was reduced by manipulation and a plaster dressing was applied and kept on for 8 weeks. The arm was markedly atrophied and remained thinner than the right one until the time of the second injury. There was no pain or other deformity, however, and the arm was used quite freely except for some slight limitation of pronation and supination. The puncture wound in the skin healed well and there were no signs of inflammation or infection.

She attended school during the autumn in good health and engaged in all of the usual activities. On February 9,

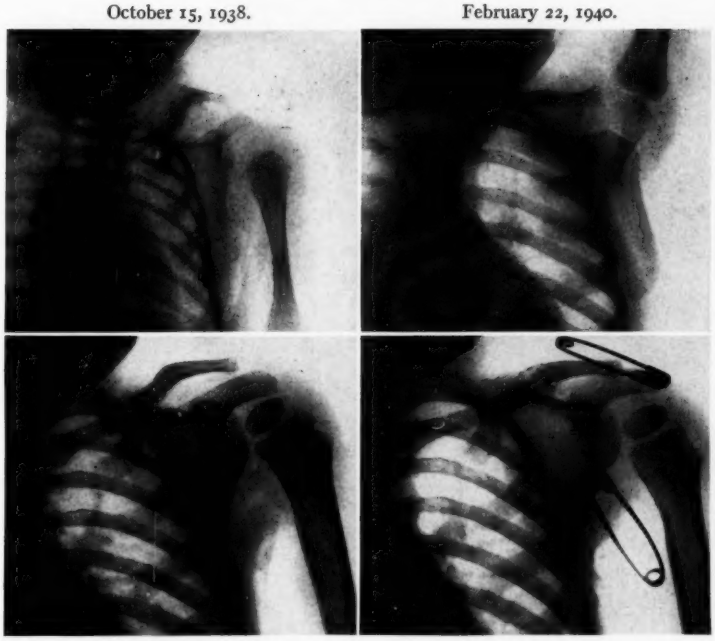


Fig. 14. Case 12. Recurrent fracture of the clavicle in a 2 year old boy after an interval of 2 years and 2 months. The first fracture occurred at birth and was observed to have healed without deformity in a study of the chest on February 22, 1940. The peculiar character of the second fracture line is well shown.

1941, she went skiing and again injured the left forearm. X-ray studies on the same day showed new fractures of both radius and ulna at the old fracture sites. There had apparently been complete healing at the old fracture sites with the formation of dense bone. The recent fracture lines had a different character and configuration than the first ones and resembled those seen in "brittle bones." Whereas the first fracture of the ulna was oblique the present one was transverse. No disalinement was demonstrable at this time except for the slight angulation of the ulnar fragments toward the radius with the former fracture well healed.

At an interview on March 10, 1941, she was seen to be a rather thin and pale girl weighing 46 kilograms with a height of 164 centimeters. There was an unusual degree of mobility at the joints but the sclerae were white and there was no deafness. Her mother described her appetite as very poor and she had always been smaller for her age than her two sisters. She disliked meat and could not eat eggs. There was a moderate intake of milk and fruit and small amounts of vegetables. The only fracture other than those described was one involving the right clavicle at the age of 7. No fractures had been experienced by the two sisters or either parent.

Case 11. R. DeT., C. H. F 8266. This boy was born of Italian parentage on October 5, 1931, and on December 1, 1940, while sledding placed his extended left arm against a tree to avoid hitting it and felt something snap. There was considerable deformity of the forearm and the x-ray examination a few hours later revealed fractures in the middle thirds of the radial and ulnar shafts (Fig. 13). After several attempts at manipulation over a period of 6 days, the fragments were finally brought into a satisfactory position and alinement, as viewed in both planes. The history and physical examination at this time disclosed that he had been breast fed in infancy and had had no cod liver oil and very little orange juice. The tonsils were described as large and irregular and the teeth poor. There was no anemia—hemoglobin 13.7 grams/100 cubic centimeters—and the tuberculin and Kline tests were negative. The elbow and wrist joints were immobilized in plaster until February 4, 1941, and the arm was kept in a sling for another 2 weeks. The x-ray examination of February 4, 1941, showed the alinement excellent in both planes with solid bony union occurring at both fracture sites. On March 11, 1941, the fracture was considered healed with a "good result."

The arm was used without pain or disability and neither the child nor his mother observed any difference in the size or alinement of the two arms. In March he played baseball pitching for a 4 man team which won the game. He also engaged in other sports, especially fighting, and his mother stated that he was always active as before. On April 8, 1941, while chasing a girl in a fight at school, he fell on his outstretched left arm and sustained another injury. X-ray studies showed new fractures of the radius and ulna at the old fracture sites. The character and configuration of the fracture lines were quite different at this

March 23, 1939. May 3, 1939. February 15, 1941.

Fig. 15. Case 13. Recurrent fracture of the clavicle occurring in a 4 year old girl after an interval of 1 year and 11 months. There was a temporary deformity at the first fracture site but healing at the time of examination was apparently complete and there was no evidence of disability present.

time, however. The bone, although dense, appeared to lack a normal structure and the appearance of the fracture lines indicated an increased fragility.

At an interview on April 19, 1941, he was seen to be an active child with thin, wiry extremities. There was a little more than the usual flexibility of the ligaments about the joints and the sclerae were distinctly bluish, but there was no deafness. He weighed 26 kilograms and measured 127 centimeters in height. He had had no other fractures than those described and none was known in the parents or 4 other siblings. His mother described his appetite as good, with a generous intake of eggs, vegetables, and meat, with fruit of some kind daily.

Case 12. M. L., C. H. D 9432. This boy was born of Sicilian parentage on October 2, 1938, as one of a pair of twins. There was a cephalic presentation and delivery seemed to be uncomplicated, but 2 weeks later a deformity of the left clavicle was noted. The x-ray examination on October 15, 1938, showed a fracture without displacement of the fragments in the middle third of the clavicle with a large amount of callus at the fracture site. No treatment was advised, and in due course complete recovery occurred with free use of the arm and no sign of discomfort.

He suffered from frequent upper respiratory infections and was seen many times on this account in the Out Patient Department. On March 6, 1939, he fell about 3 feet, sustaining a fracture of the right parietal bone. Recovery was complicated by mastoiditis for which a bilateral mastoidectomy was performed. On February 22, 1940, in the course of an upper respiratory infection, an x-ray study was made of the chest which incidentally revealed complete healing with a normal appearance of the bone

June 20, 1933. November 24, 1939.

Figs. 16, above, and 17, right. Case 14. Recurrent fracture in the proximal metaphyseal area of the right tibia in an 8 year old boy, 6 years after the original fracture. Although the fracture sites appear to be identical the bone structure at the first fracture site has gone to form the cortex of the shaft and as the result of the growth of the bone lies some distance distal to the second fracture site.

June 20, 1933. November 24, 1939.

Fig. 17.

(*Legend in left column.*)

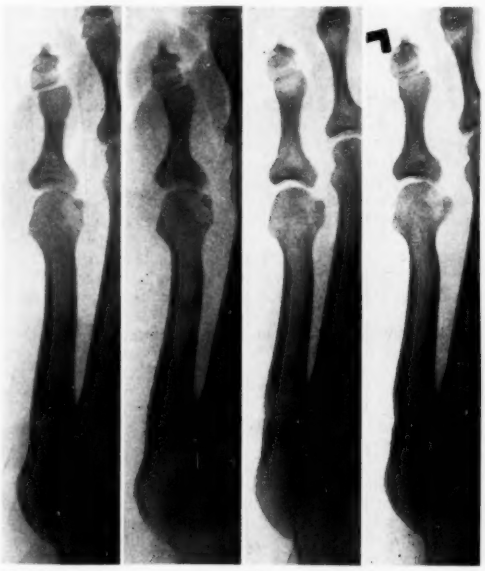
structure and no deformity at the old fracture site in the left clavicle.

On December 11, 1940, he tripped while running with his twin brother and fell on his left shoulder with his arm beneath him. There was evident pain on lifting his left arm. An x-ray examination on the same day revealed a simple transverse fracture line at the old fracture site. Any question as to the presence of a recent injury was answered by a re-examination on January 4, 1941, which showed a large amount of soft callus at the fracture site.

At an interview on this date the child was found to have a weight of 10 kilograms for a height of 83 centimeters. He seemed well nourished and his appetite was said to be excellent for a variety of foods. He had sustained no fractures other than those described and no fractures were recalled in the parents or in five siblings with the exception that one other child had sustained a fracture of the clavicle at birth. The sclerae were distinctly bluish and there was considerable flexibility of the ligaments but no sign of deafness.

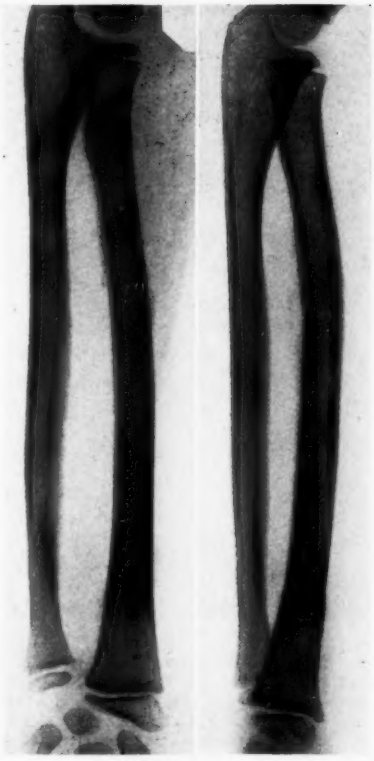
CASE 13. B. A., C. H. E 2202. This girl was born of Polish parentage on August 5, 1937, and was first seen at the Children's Hospital on March 22, 1939, following a fall on some steps which produced an injury to the right shoulder. The roentgen-ray examination demonstrated a fracture of the clavicle near the junction of the proximal and middle thirds with the usual deformity. A dressing was applied for immobilization and maintained for 6 weeks. At the roentgen-ray study of May 3, 1939, it was observed that osseous union was occurring with a large amount of dense callus and with some overriding of the fragments, the distal end of the proximal fragment being displaced upward. After the dressing was removed, the child favored the right arm for a short period but she soon exhibited her normal right handedness, and there was no complaint or disability of any kind. The mother noted a lump at the fracture site but this disappeared in 1 or 2 months with no residual deformity. She experienced mild whooping cough in the spring of 1939 and chickenpox in the summer of 1940. She had suffered from eczema since birth and at 1 year of age was placed on a vegetable-poor diet for 6 months without benefit. There had been occasional colds and on December 24, 1939, she was hospitalized for nasopharyngitis, otitis media, and cervical adenitis.

On February 14, 1941, she fell from a couch and sustained a heavy blow to the right shoulder. Roentgen-ray study revealed a new fracture without displacement or disalinement of the fragments at the old fracture site. There was otherwise a normal appearance of the bone structure and the old fracture had apparently healed completely and without deformity.



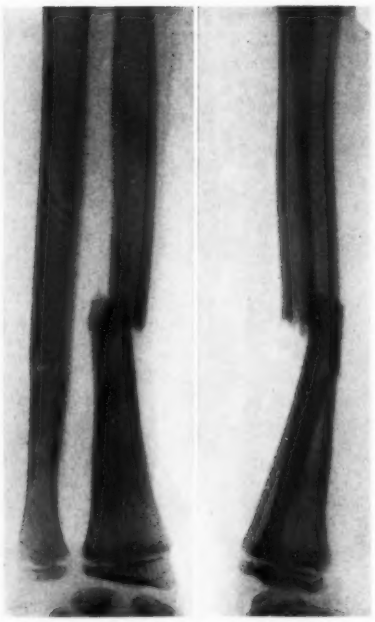
April 5, 1937. February 7, 1938.
September 22, 1937. September 7, 1940.

Fig. 18. Case 15. Two recurrent fractures in the shaft of the fifth metatarsal bone of an obese, 18 year old boy, after intervals of about 5 months during which healing appeared complete. Each fracture was immediately preceded by an acute, severe trauma and the fracture lines have a slightly different character and configuration.



July 26, 1940.

Fig. 19. Case 16. Two views of the right forearm of a 6 year old boy showing a recent fracture of the radius near the junction of its proximal and middle thirds and the dense bone structure at the site of a fracture which had occurred 10 months before. The first fracture was in the distal third and cancellous portion of the diaphysis.



September 5, 1940.

Fig. 20. Case 17. Two views of the right forearm of an 11 year old negro boy showing recent fractures in the middle thirds of the radius and ulna with dense bone structure in the cancellous portion of the radius proximal to the distal epiphysis at the site of a fracture which had occurred 3 months before.

At an interview at the time of the second fracture she was found to weigh 15.5 kilograms with a height of 95 centimeters and appeared well nourished although her mother said she had a poor appetite. She disliked meat but would eat milk, eggs, and vegetables. She was described as being very active with many falls and bruises but rarely any serious injury. She had sustained only the two fractures described, and there was no history of fracture in the parents or sister. The sclerae were considerably bluish but there was normal flexibility at the joints and no deafness was evident.

CASE 14. H. S., C. H. 89110. A Jewish boy born on October 30, 1931, was seen in the Children's Hospital in 1931 and 1932 for various minor complaints including a feeding problem. On June 18, 1933, he fell from a parked automobile and the right knee was noted to be tender. X-ray examination revealed a greenstick type injury of the tibia just beneath the proximal epiphyseal line (Fig. 16). There was no significant displacement or disalinement of the fragments and a plaster cast was applied. Due to the mother's illness the child was not brought back for further care. After 6 weeks the cast fell off spontaneously. "Sores" and "big blisters" were seen on the leg and foot, and after many months of household remedies healing took place and normal use of the part was obtained. He became a very active child, indulging in violent games and sustaining many mild injuries. In August, 1937, he was treated for a limited injury at the lower end of the left radius.

On November 24, 1939, while playing football, he fell striking a rise in the ground and again injured the right knee area. X-ray studies showed fracture lines at the proximal end of the tibial diaphysis in otherwise apparently normal bone structure. Healing took place in a satisfactory manner with no resultant deformity or disability.

At an interview on November 30, 1940, he was observed to be a well developed and nourished boy, weighing 29 kilograms and with a height of 132 centimeters. His mother stated, however, that he had been less well nourished in the past and was a "fussy" eater, usually going without breakfasts and eating very little meat. The only other history of fracture in the family was in one brother who had sustained two fractures of the forearm. The patient's sclerae appeared normal and there was no deafness or hyperextensibility at the joints.

CASE 15. A. G., 18 years of age, a private patient of Dr. J. O. Kopel. In April, 1937, while playing baseball, he turned his foot on first base. He was able to walk for 2 to 3 days but with much pain and on April 5, 1937, x-ray studies (Fig. 18) were made, revealing a fracture at the base of the fifth metatarsal bone. A plaster cast was applied for 3 weeks, and subsequently he was able to walk without disability.

In September, 1937, on jumping over a wire he felt something snap in the left foot. X-ray studies showed a new fracture in the fifth metatarsal bone and a cast was applied for 4 weeks. There was satisfactory recovery and he was able to walk without pain or other disability.

One night in February, 1938, he injured his left foot for the third time when he tripped over a wire in the dark. X-rays again showed the appearance of a new fracture and a cast was applied for 4 weeks. Recovery was satisfactory as before.

When interviewed in September, 1940, he was having no pain or difficulty in walking and roentgenograms revealed complete healing of the old fractures. He was observed to be a large, obese boy weighing 104 kilograms with a height of 185 centimeters. There was no deafness and the sclerae were white but there was somewhat more than the usual mobility at the joints. He was not aware of having sustained any other fractures than those described in the left fifth metatarsal bone.

CASE 16. R. G., C. H. D 6150. This boy, born on June 15, 1934, fell 3 or 4 feet to the ground from a porch on September 19, 1939, and sustained an injury to the right lower forearm. A diagnosis of fracture was made by the family physician without an x-ray examination and splints were applied for 4 weeks. A good result was obtained with no further trouble until July 12, 1940, when he fell on his outstretched arm and hand while playing on a tree stump and again injured the right forearm. Pain persisted and a small area of ecchymosis appeared. An x-ray examination (Fig. 19) at the Children's Hospital 2 weeks after the injury revealed evidence of the old completely healed fracture at the lower end of the radial diaphysis and a more recent fracture of the radial shaft near the junction of the proximal and middle thirds. A plaster dressing was applied and retained for about 3 weeks, and the normal use of the arm was regained.

CASE 17. R. G., C. H. 70549. A colored boy born of syphilitic parents on June 24, 1929, was seen in the Children's Hospital on many occasions for minor complaints. On June 10, 1940, he fell on his right hand and a greenstick fracture at the lower end of the radius, 2 centimeters proximal to the lower epiphyseal line, was demonstrated by x-ray. There was slight buckling of the cortex posteriorly but there was no important displacement or disalinement. Treatment consisted in immobilization in plaster for a

number of weeks and a satisfactory result was obtained. On September 5, 1940, he fell on his outstretched hands while riding a bicycle and felt a sharp pain in the right forearm. X-ray studies showed complete healing at the old fracture site with new fractures in the shafts of the radius and ulna near the junction of their middle and distal thirds. After unsuccessful attempts to reduce the deformity by manipulation, an open operation was carried out with a satisfactory approximation of the fragments and a good final result.

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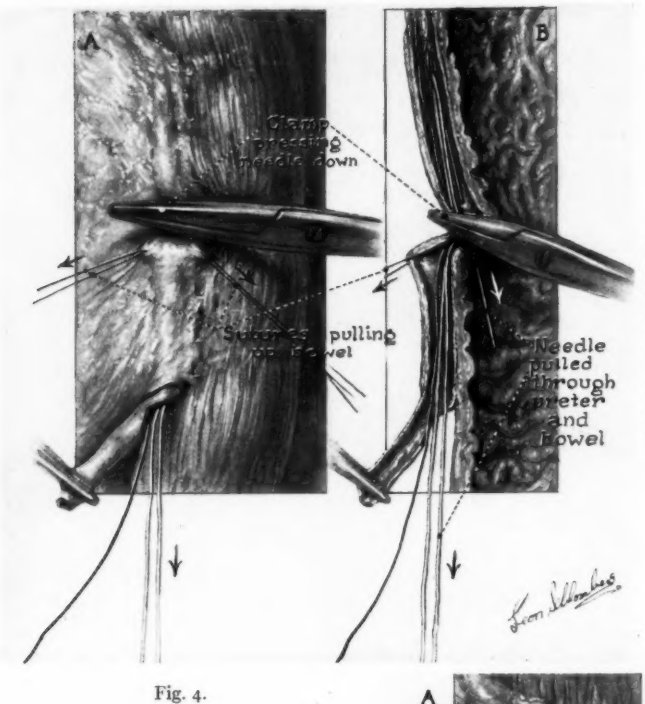

Fig. 4. The mechanism by which the needle is forced through the wall of the ureter and through the submucosa and mucosa of the bowel into the lumen of the rectosigmoid. This is accomplished by pulling up on the two temporary traction sutures placed on either side of the embedded ureter, pressing down with a clamp over the point of the needle and, with traction on the braided silk suture in the eye of the needle, the point of the needle is forced through the intervening tissue into the lumen of the bowel.

Fig. 4.

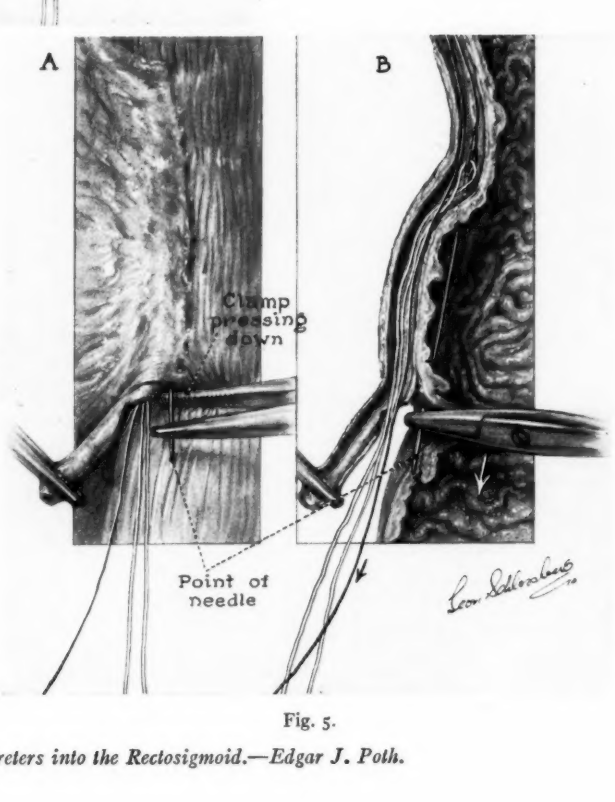

Fig. 5. The needle emerging from the bowel. It is grasped with a clamp and the traction suture is pulled out of the eye of the needle.

Fig. 5.

Implantation of Ureters into the Rectosigmoid.—Edgar J. Poth.

IMPLANTATION OF URETERS INTO THE RECTOSIGMOID WITH A STUDY OF THE POSTOPERATIVE COURSE

EDGAR J. POTH, Ph.D., M.D., Baltimore, Maryland

DURING the past few years, numerous attempts have been made to improve upon old methods (5) and to devise new techniques (1, 3, 4, 6, 9) for the implantation of ureters into the rectosigmoid. Obviously, it is unphysiological to divert the urinary stream into the large bowel where the normal constituents of the urine will be acted upon by the ferments and bacteria of the intestinal tract. However, one is forced to form this outlet in certain instances of developmental anomalies of the bladder, or in cases in which the bladder must be removed because of malignancy or other disease.

The most important considerations in such an implantation are that the opening of the ureter into the bowel be adequate, pliable, and free of surrounding fibrosis, and that the ureter lie in the wall of the bowel for a distance before opening into the lumen of the intestine. Coffey demonstrated that this intramural segment acts as a check-valve to prevent the retrograde passage of material up the ureter when the bowel contracts. Since the intestinal contents are liquid after the implantation of the ureter and the delivery of urine into the intestine, it is particularly important that this valve functions well so as to exclude the highly infectious material from the urinary tract. The most efficient check valve is ensured when healing between ureter and bowel occurs in a surgically clean bed, which is accomplished in a technique described by the author. The ureter has a fibrous tissue covering which is laid directly on the fibrous submucosa of the intestine. Infection in such an anatomical environment predisposes to excessive development of scar tissue, which will result in a stiff intramural tube, and will function poorly as a check valve against retrograde flow of fluid into the ureter. Furthermore, during the healing following the first stage, there is edema of the tissues involved, and they cannot respond to changes of pressure in the bowel. During this 10 day period it is important that the ureter shall not be open into the lumen of the bowel, if retrograde passage of contaminated material up the ureter is not to occur and initiate a serious infection of the upper urinary tract. To have a properly functioning valve is considered of sufficient importance to justify an additional operative procedure when possible. The operation of implantation of the ureter is divided into two stages; in the first stage the ureter is embedded in the wall of the bowel without interruption or diversion of the urinary stream, and in the second stage the opening is made between the ureter and the bowel with diversion of the urinary stream into the intestine.

This unphysiological formation of a cloaca gives rise to a number of abnormalities, especially in the dog. Since this animal stands on all fours, his large bowel is in a practically horizontal position, and this position, coupled with the fact that in

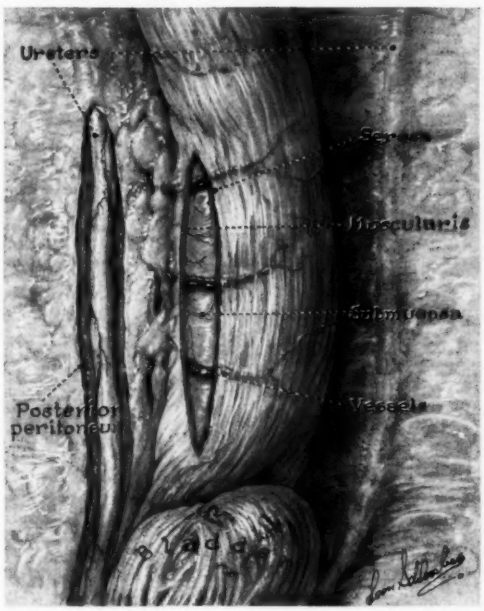

Fig. 1. First stage. Illustrates incision of rectosigmoid down to submucosa with the preservation of the blood vessels, and shows the right ureter exposed and developed for implantation into the bed in the bowel.

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The major portion of this work was done in the Department of Surgery, Stanford University School of Medicine, San Francisco, California.

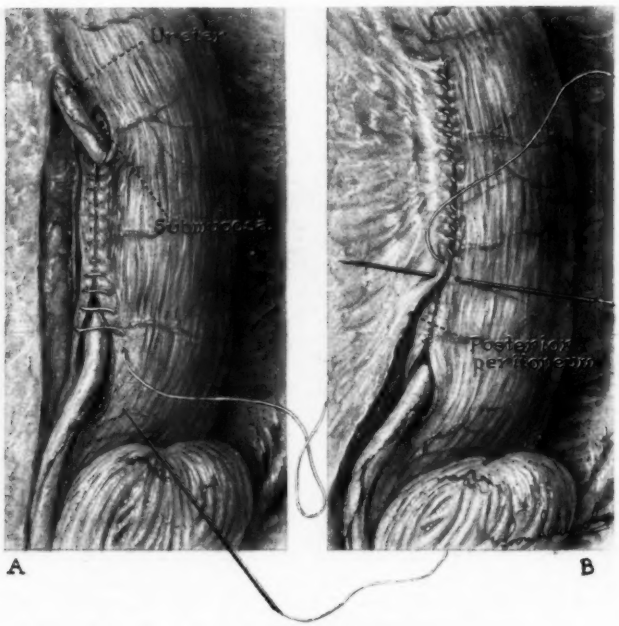

Fig. 2. First stage. *a*, Method by which the ureter is embedded into wall of bowel by means of a continuous Lembert or Cushing suture of No. 0 chromic catgut. Submucosa is left showing at both ends to avoid compression of the ureter. *b*, Manner in which cut edge of peritoneum is sutured over the implanted ureter. This obviates kinking of the ureter as it goes from its usual retroperitoneal location to its new bed in the wall of the rectosigmoid. Two weeks are allowed for healing before the second stage of the operation is undertaken. Silk should not be used to close the intestinal bed because it frequently cuts through the underlying ureter, even though interrupted sutures are employed.

the dog the large bowel has no well developed valves or folds but is rather a straight tube, allows the fluid material resulting from the admixture with urine to flow upward to the ileocecal valve or even higher and gives rise to much reabsorption. This reabsorbed material appears to be rather toxic and results in a secondary anemia.

OPERATIVE PROCEDURES

In the course of this and previous studies numerous operative techniques have been used. When the single stage procedure is used in which the ureter is embedded in the wall of the bowel and the opening between ureter and bowel is made as advocated by Coffey, Mayo, and Hinman (6), the survival rate is 5 to 10 per cent if both ureters are embedded at the same time. Death results from leakage, infection of the operative bed, and peritonitis. In my hands, with the technique advocated by Higgins, there was a mortality of approximately 25 per cent in the first stage from leakage and infection. The mortality in the two stage procedure previously described by the author and the modification here presented was less than 5 per cent in the experimental animal. These deaths were not due to leakage, infection, or peritonitis, but were due to the small size of the structures, resulting in technical difficulties and tearing of the ureter. Although the technique originally described by the author is entirely satisfactory for the experimental animal, it cannot always be applied to the human being, because the pressures of large tumors in the bladder or elsewhere pressing on the bowel may make it impossible to pass the proctoscope in the second stage. Although this technique is preferred whenever it is applicable, a second method has been developed for those cases in which the proctoscope cannot be inserted. The first stage is

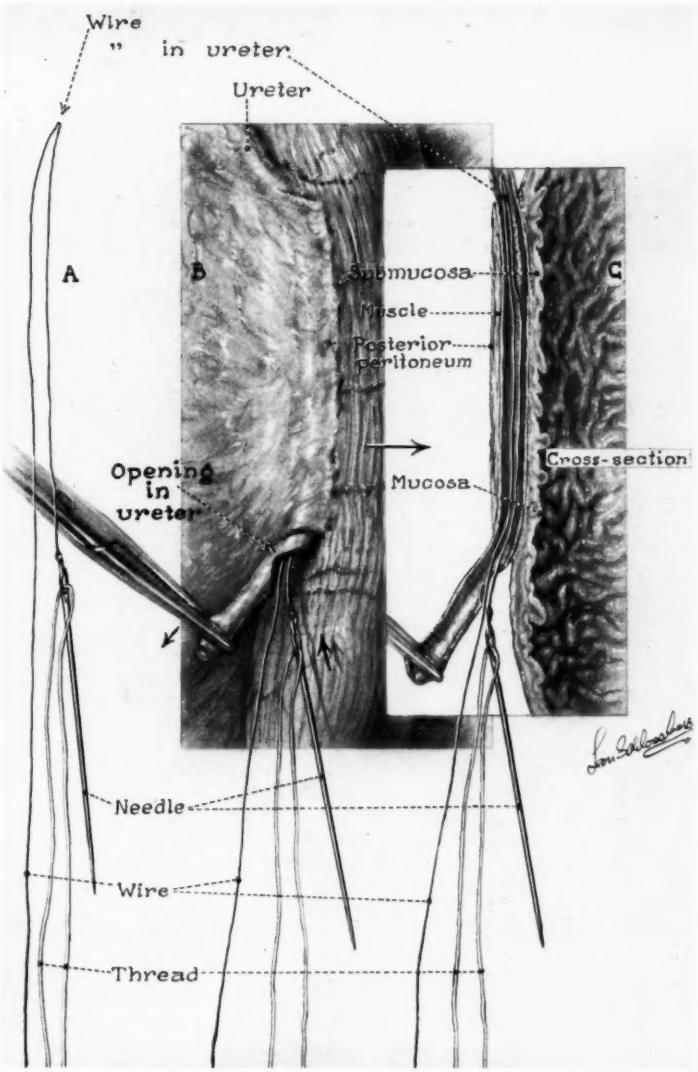

Fig. 3. Second stage. Two weeks have elapsed between first and second stages to permit aseptic healing of the ureter in its intramural location. *a*, An assembly of the cutting device consisting of a heavy darning needle mounted with a length of No. 26 B & S gauge nichrome wire and a traction suture of fine braided silk. This will serve as the cutting instrument to connect the lumina of ureter and bowel. *b*, The cutting assembly being introduced into the ureter. *c*, Same as b in cross-section.

essentially unchanged. The second stage is not an entirely aseptic procedure; however, the most important healing of the ureter in its intramural bed has already occurred in a clean field. If gross soiling should occur at the second stage, the bladder should be removed at a later date. The operation of ureteral transplantation on a debilitated human being is a considerable undertaking, and

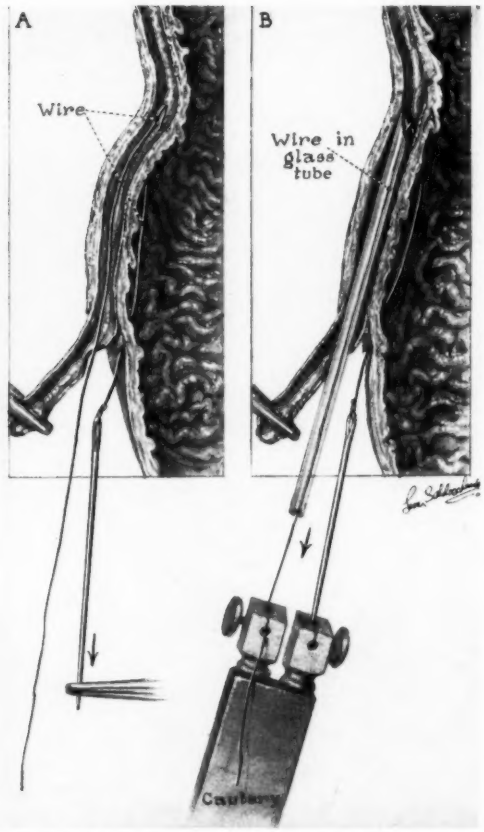

Fig. 6. A heavy walled glass tube placed over one limb of the cautery to protect the ureter. A high cautery current is used in order that cutting will proceed rapidly as the instrument is withdrawn. The wire has been placed to cut a slit about 1.5 centimeters long connecting the ureter and bowel.

one should be prepared to perform it in multiple stages and not to do too much at one time. The technical procedure can be readily followed in the illustrations.

THE UNPHYSIOLOGICAL STATE

Again it must be said that the dog is a poor experimental subject for ureterointestinal anastomosis. He walks on all fours, there are no valves in the large bowel, and he has a strong anal sphincter and a heavy, well developed bowel musculature. The heavy bowel musculature causes a slight dilatation of the ureter above the implantation. This dilatation and obstruction is not sufficient to be demonstrable by intravenous

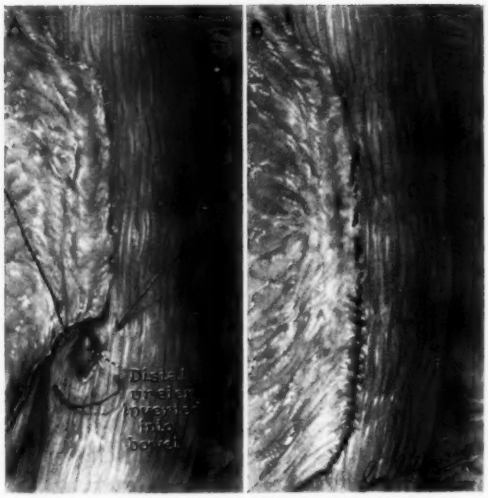

Fig. 7. The incision completed, the distal end of ureter is ligated, cut short and inverted into bowel. The opening in the bowel is ordinarily closed with a single matress suture. The area is covered with peritoneum as indicated.

urography. This change, moreover, is not due to the ureter's being subjected to the intraintestinal pressure, because it develops even though the first stage only is done. The anthropological and anatomical arrangement of the dog favors excessive absorption of the urinary constituents from the bowel following ureterointestinal anastomosis. It is likely that some of the substances contained in the urine are altered by the bacterial flora and the ferments in the bowel before they are reabsorbed. After transplantation of the ureters into the rectosigmoid the excrement from the bowel has a strong ammoniacal odor.

Although it has not been proved, it is believed that the ammonia liberated by the urease acting on the urea of the urine excreted into the bowel is absorbed and acts as the toxic substance. A secondary anemia develops which does not seem to result from the increase in blood urea *per se*. The usual course of blood urea and hemoglobin levels are illustrated in Figure 8. Within 2 weeks after the first stage of the operation, nonprotein nitrogen blood level and the hemoglobin return to normal and would remain unchanged indefinitely. Following the second stage, however, when urine is being discharged into the bowel, there is a moderate and immediate rise in the nonprotein nitrogen level of the blood. After this immediate change the percentage of nonprotein nitrogen remains essentially constant, except for occasional

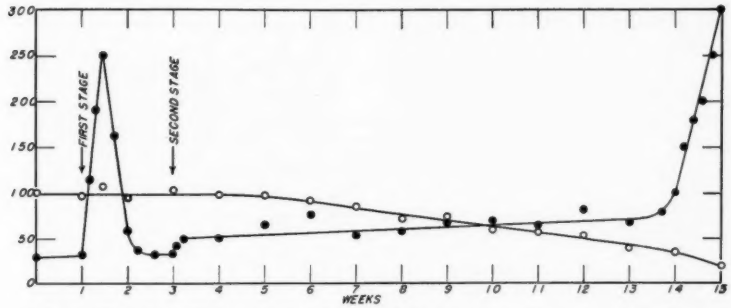

Fig. 8. This chart illustrates the characteristic course of the nonprotein nitrogen (solid dots—mgm. per cent) and hemoglobin levels (circles per cent) as observed in a series of 44 animals. Eventually all animals die following a sudden rise in nonprotein nitrogen and rapid fall in hemoglobin. Animals frequently survive for 6 to 8 months.

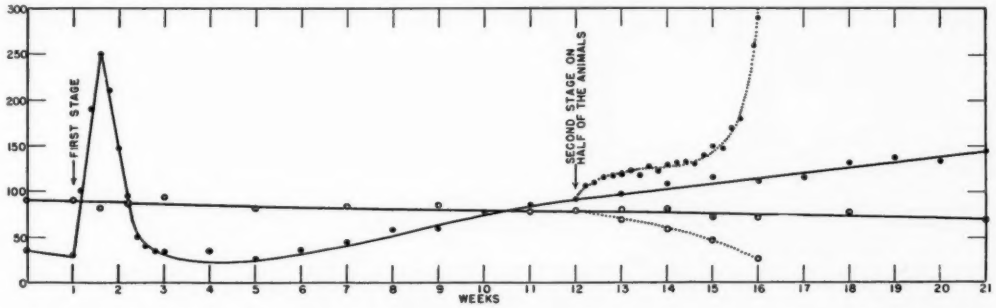

Fig. 9. This chart illustrates the characteristic course of the nonprotein nitrogen (solid dots) and hemoglobin levels (circles) as observed in a series of 20 animals. Half of these animals were subjected to the first stage of the operation only, and the other half were operated upon twice as indicated, and their subsequent course is plotted by the dotted lines. The sudden increase in nonprotein nitrogen and the rapid decrease in hemoglobin occur only when the second stage of the operation is done and urine is delivered into the large bowel. In all of these animals loose bands of cellophane or silk were placed around both ureters at the time of the first stage of the operation. These bands caused a gradual constriction of the ureters of the dogs. Animals have been known to tolerate for long periods of time a high nonprotein nitrogen blood level that is caused by simple obstruction.

periodic fluctuations, until the development of a rather severe secondary anemia. Following the establishment of an opening between the ureter and the bowel, the hemoglobin falls progressively and at a regular rate until it reaches 40 to 50 per cent. Up to this time the animal appears normal. There is then a sudden change; the animal refuses to eat, the rate of the hemoglobin fall increases, and the nonprotein nitrogen rises abruptly. Death, frequently accompanied by a Bacillus coli septicemia, occurs within a week. Necropsy shows the opening between ureter and bowel to be patent and soft, and the upper urinary tract is essentially normal both grossly and microscopically. Apparently the fall in hemoglobin is not dependent upon the nonprotein nitrogen level of the blood. In a group of 20 animals bands of cellophane or silk were, at the time of the first operative stage, placed loosely around both ureters proximal to the implant. These animals show the usual immediate elevation of blood urea, with return to normal for a period of weeks; and then, with the gradual development of fibrosis in the region of the bands and constriction of the ureters, the nonprotein nitrogen of the blood rises slowly to high levels. During this time there is but a slight drop in hemoglobin. If on alternate animals, however, the second stage of the operation to deliver urine into the bowel is performed, the courses followed by the two groups are entirely different. From the difference in the blood pictures of the two groups, as illustrated in Figure 9 it appears that the nonprotein nitrogen blood level is not responsible for the anemia, but rather that substances are being absorbed from the bowel which react to cause this and other changes.

Whether this intoxication is due to the absorption of ammonia from the bowel for resynthesis into urea by the liver, which in turn is re-excreted by the kidney to establish a vicious cycle, has not been proved but is postulated as a possible, reasonable explanation of the anemia and the death of the animals.

EVALUATION

The marked rise in blood urea following the bilateral embedding of ureters in the first stage demonstrates conclusively that both ureters should not be embedded simultaneously in a debilitated person with a high initial blood urea. If preoperative intravenous urography shows the ureters to be greatly dilated, it must be appreciated that these enlarged structures cannot be successfully buried in the wall of the bowel. Under these circumstances it is well to consider nephrostomy as recommended by Cabot and to allow sufficient time for the ureters to decrease in size and for the kidney function to improve. Nephrostomy followed by the simultaneous embedding of both ureters is a simpler, safer, and more satisfactory procedure than dealing with the ureters singly. The use of ureteral catheters during this period has been suggested, but this may be impossible mechanically, and catheters are poorly tolerated in the presence of the infection frequently found in urinary stasis.

In view of the rise of blood urea and the fall of hemoglobin and their apparent association with the reabsorption of toxic products following the delivery of urine into the rectosigmoid, it is suggested that the patient be placed in the semi-Fowler position as soon as practical after operation, that a small rectal tube be inserted just beyond the sphincter ani, and that he be encouraged to evacuate the bowel frequently. Jewett incised the anal sphincter of dogs to facilitate emptying the bowel.

Frequent hemoglobin determinations should be done. While in bed, the patient should assume the semi-Fowler position and be awakened once at night to empty the bowel. Mild catharsis may be indicated.

It cannot be repeated too frequently that the healing following embedding of the ureter in the wall of the bowel should occur in the absence of infection in order to ensure a patent orifice and a soft, readily compressed intramural bed for the ureter.

SUMMARY

1. An alternative procedure is presented for the second stage of the operation for ureterointestinal anastamosis.

2. The unphysiological state created by the formation of an abnormal cloaca is discussed.

3. A secondary anemia following ureterointestinal anastamosis is reported.

4. The cause of late death of the experimental animals is considered.

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INTERNAL WIRE FIXATION FOR FRACTURES OF JAW

Preliminary Report

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IN some fractures of the lower jaw, in which interdental wiring cannot be done, a wire—of the Kirschner type—drilled across the fracture line may be an easy and satisfactory method of treatment.

The indication for this internal fixation may be present when the opportune early time for interdental fixation has passed and the fragments have become displaced, with compounding into the mouth, infection, and local sloughing. It also may be considered in edentulous jaws; when there is much comminution and accompanying injury, as in gunshot and war injuries; when many teeth have been loosened or broken; in displaced symphysis fractures; and in fractures at the angle in which the posterior fragment is pulled out and up into the upper buccal fornix by the closing muscles (Fig. 3). This last deformity is one of the worst to contend with, and, if left uncorrected, may result in non-union of the fragments. It may also prove to be of value in certain separations of the upper jaw.

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Fig. 1. Bad comminution at symphysis with only small points of bone in contact, left condyle and many teeth broken. Fixation at symphysis with one internal wire and a second plane of fixation obtained with an anterior wire arch. Jaws wired together because of the condyle fracture opened after 4 weeks with internal wire still in place.

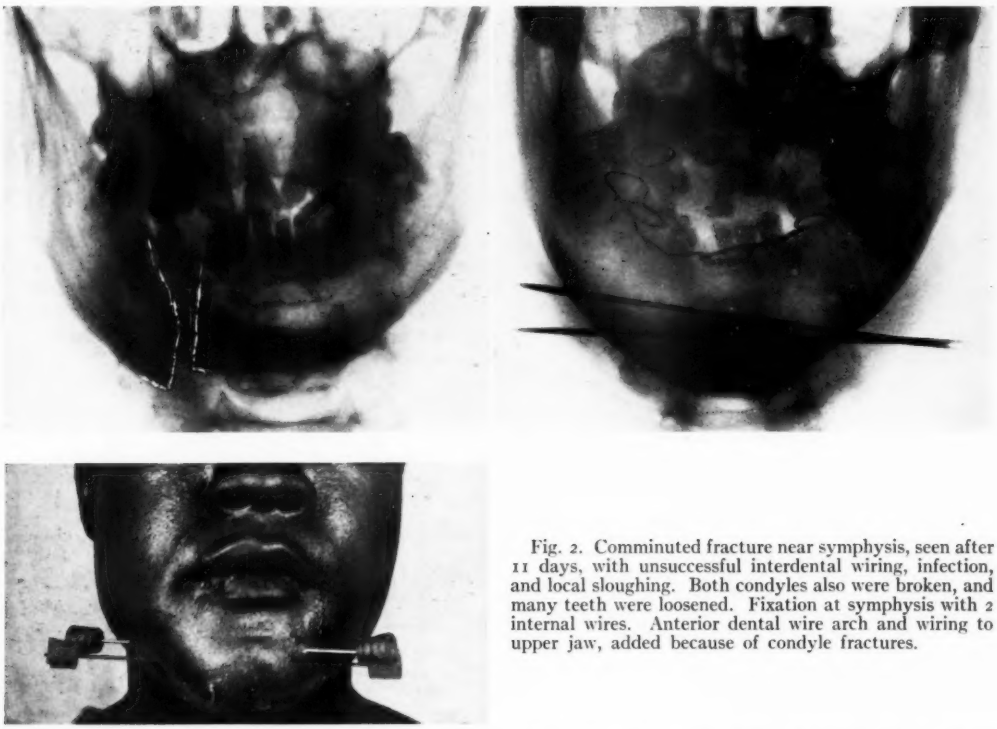

Fig. 2. Comminuted fracture near symphysis, seen after 11 days, with unsuccessful interdental wiring, infection, and local sloughing. Both condyles also were broken, and many teeth were loosened. Fixation at symphysis with 2 internal wires. Anterior dental wire arch and wiring to upper jaw, added because of condyle fractures.

The internal wire will insure fixation in one plane, —that is, the fragments cannot slip up or down past each other. However, they might rotate, in or out, or they might pull apart and, therefore, *the addition of an anterior wire dental arch* will give a second plane of fixation that will prevent rotation and will jam the fragments in impaction so that separation will not occur. If there is a condyle fracture to deal with also, or if normal occlusion cannot be maintained, then there can be the *further addition of interdental fixation to the upper jaw.*

Multiple internal wires can be used for multiple fractures, or to give the second plane of fixation if desirable.

Avoidance of the nerve canal is advisable even though the nerve may have been cut in two by displacement of the fragments. The same is true of any good teeth and this can usually be done by staying below the canal. When a second wire is placed above the lower one, there is more chance of damage of the nerve and teeth.

An electric power drill is practically necessary, as the hand drill may not give enough speed for easy penetration of the bone. Regular Kirschner wires may be used, but stainless steel wires, recommended by Dr. C. H. Crego in leg lengthening, are cheaper and can be obtained in suitable lengths of thickness from .05 inch to .08 inch, a three-sided point being put on them.[1] Bicycle and velocipede spokes also have been used by Dr. Crego.

A further modification is to cut threads all the way along an .08-inch wire with a 2-56 die, which is a bicycle spoke threader, and, after it has been drilled into position, screw regular bicycle spoke nipples or small nuts down against the bone to hold the fragments together. This threaded wire itself may give sufficient tightness without the nipples to prevent separation and is applicable in edentulous patients or any time the dental arch cannot be used (Fig. 4).[2]

OPERATION

Local or deep block anesthesia is usually employed. The fragments are alined with the hands,

[1]This wire is 18-8 stainless steel. The smallest size to give the necessary stiffness is preferable.

[2]It has been [suggested by Dr. J. A. Brown that the threaded wires might be omitted and where fixation against the bone is desired, a hollow cylinder could be slipped over an unthreaded wire down against the bone and held with a set screw put in the end of it.

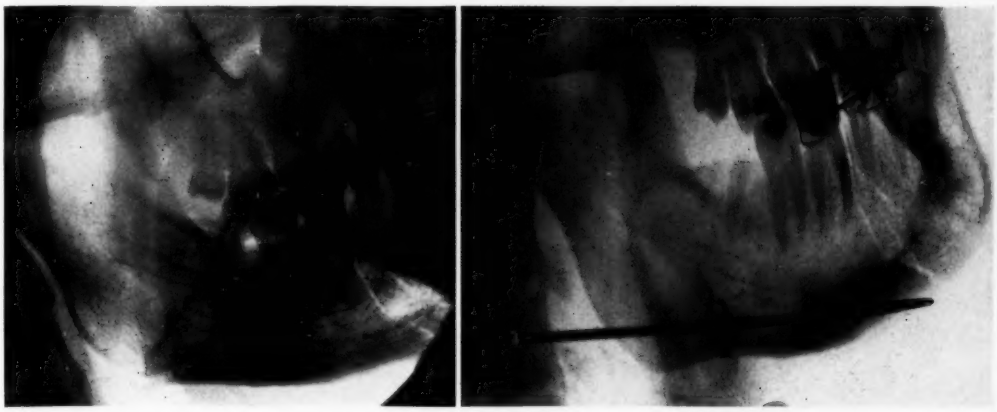

Fig. 3. Fracture at angle with elevation of posterior fragment and loss of mandibular nerve sensation. Fixation with single internal wire put in from behind and below the nerve canal. Avoidance of open reduction or elastic traction reduction of posterior fragment. Interdental wiring was done because of second fracture in body. At right, mouth open, with wire in place.

or an open reduction may be necessary, an elevator being used between the fragments. It is important that reduction be accurate, as only slight adjustment is possible after the wire is in.

A puncture incision is made to get the wire in against the bone, and the wire and drill are lined up accurately. Then, perhaps most important of all, the fragments have to be held in accurate position with the hands while the wire is drilled into place. (Little mention need be made of the necessity of care with the drill and wire, and for avoidance of injury to the hands that are holding the fragments.) The wire usually is drilled on through the bone and a small opening is made to let it through the skin on other side. Secondary internal wires may be needed occasionally (Fig. 2).

The anterior arch wire is applied by putting No. 26 stainless steel wires on posterior teeth on each side, twisting the strands tightly for 2 inches, then twisting them together in midline and holding them with individual No. 28 wires around separate teeth. Any other type of arch appliance may be used, but this one requires no added equipment and is usually satisfactory.

This is the wire that should suffice for the second and final plane of fixation and should impact the fragments together over the internal wire (Figs. 1, 2, and 4).

Interdental fixation is done as mentioned, if there is some final adjustment of occlusion to be secured or if the condyles also have been fractured. The jaws may be fastened directly together or by any effective method of elastic traction.

In edentulous jaws, when dental plates wired or bandaged in place with the mouth closed will not suffice, a single internal wire or a threaded one as shown in Figure 4 may be effective as the jaws are usually small from atrophy anyway. This plan for edentulous jaws seems much less trouble for the patient and surgeon than attempting any rigid fixation within the mouth with screws down into the bone and nerve canal.

Sulfanilamide is used locally in all open wounds and right in the fracture line if it has been separated widely enough to admit the powder. Wounds of the mouth, jaw, and neck, with their marked tendency to infection, make a field of great importance for the use of this drug.

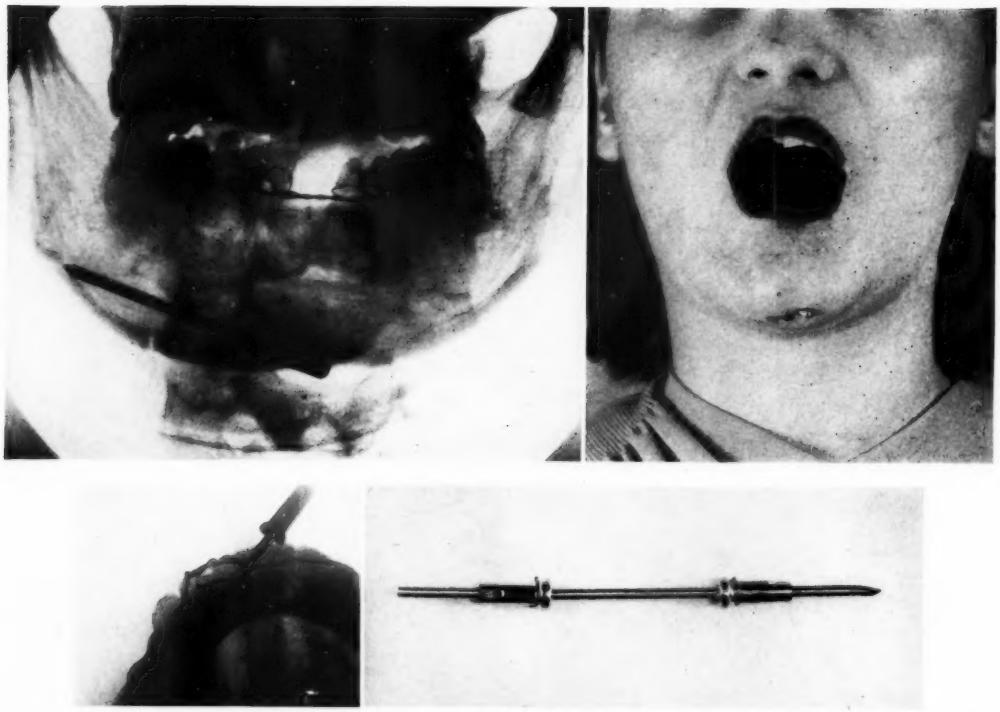

Fig. 4. 18-8 stainless steel wire .08-inch threaded with a 2-56 die-cutter which is a bicycle spoke-threader and with regular bicycle spoke nipples screwed on. (Equipment, courtesy Dr. Crego). In the patient shown the fracture is held with an internal threaded wire and one nipple. The mouth could be opened easily after the operation, and soft food was taken. Anterior arch was put on to hold a separate loose fragment.

Pressure dressings, of soft cotton mechanic's waste, are applied to give support to the soft tissues and prevent, as far as possible, hematomas, hemorrhage, and swelling, and also to lend further support to the bone fragments.

The jaw seems solid immediately and the patient experiences the usual comfort of a set fracture. The ends of the wire are covered and the patients do not object much to discomfort. In some instances, the wires may be cut short enough to be covered by the skin, but it is probable that they all should be removed finally. Just one or two days are required in the hospital, and some patients can open the jaws and take soft foods almost immediately.

The removal of the wires can be done easily after 3 to 5 weeks, depending upon the progress. There may be some irritation around the wires but no serious osteomyelitis should develop.

This plan was thought to be new, but articles on the subject were found by Ipsen and Sobye in Denmark and Meade in Ireland, and these men seem to have been the only ones to have reported it.

In the voluminous literature from the last war and since then, there has been a multiplicity of dental splints, often with emphasis on some contrivance of little fundamental bearing. If this simple direct method of internal wire fixation by drilling a wire across the fragments will help avoid the use of complicated dental splints, overhead plaster-cap traction for elevated posterior fragments, and wide open reductions, it will be worthwhile.

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REACTION OF BONE TO METALS

II. Lack of Correlation with Electrical Potentials

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EXPERIMENTS in which as many as four different kinds of metals or alloys were implanted into the femurs of cats were reported in an earlier paper (Bothe, Beaton and Davenport, 1940). Differences in electrical potentials between a number of the implants were taken *in vivo* after a postoperative survival period of about 7 months and the reaction of the bone to the various metals was studied. The correlation between electrical potentials and bone reaction was not good, and in view of the emphasis that has been given to electrolysis, it was decided to make another series of implantation experiments to test the effect of electromotive force more accurately.

Some of the more pertinent references to experimental and clinical experiences with bone reactions to metals were cited in the preceding paper, and two more which deal with electrical phenomena can be mentioned here.

Berti-Riboli (1938) measured potentials between bone and metals at three different time intervals after applying plates to the long bones of rabbits and dogs. The method of making the measurement of the electromotive force between the bone and the plate is not made clear, but the difference of potential was found to diminish with time. Copper, aluminum, stainless steel (3 kinds), duraluminum and 20 carat gold were used, and there was a difference in the rate of diminution of potential for each metal. A hypothesis was proposed that the rate of diminution was directly proportional to the toxicity of the metal.

Hudack (1940) reported on the use of high chromium, low nickel stainless steel, and emphasized the necessity of polishing and of treating alloys with nitric acid to minimize the presence of foci for electrolytic corrosion.

It has seemed to us that too much emphasis has been placed on electrical effects and too little on the more general properties of the solubility of metals in body fluids and the reaction of tissues to the dissolution products. In order to test the influence of differences in electrical potential in contrast with characteristic properties of individual metals, we have implanted two instead of four metals into each bone and have attempted to correlate reactions with electromotive force differences.

Experimental. One male and 16 female cats were used. Two implants, usually of different metals were made into each femur. The technique of making the implantation was the same as that used in the previous experiments. All 17 animals survived the experimental period, and were sacrificed at intervals between 186 and 329 days. Electrical potentials between the two implants, and also the potential from a copper electrode in the adjacent muscle to each implant, were measured while the animal was under anesthesia just prior to sacrifice. A few of the implants had become buried in the bone and potentials on them were not secured, and one had sloughed into adjacent soft tissue.

In arranging the pairs of metals, the object was to secure: (1) pairs with rather large potential differences, (2) pairs with medium potential differences, and (3) pairs with little or no potential differences. The results are listed in Table 1. A critical examination of the potential differences shows that they are not reproducible from animal to animal with the degree of accuracy that might be desired, but that the order of magnitude permits them to be grouped into low, medium, and high. The potentials have been correlated with the amount of bone reaction, and a recapitulation of the findings made in Table II.

RESULTS

It is seen in Table II that 7 of the metals or alloys reacted in the direction of their electrical differences while 10 did not. This is interpreted to mean that there is no direct correlation between a condition which predisposes to electrolysis and one which does not. Reactions occurred in the regions immediately surrounding the offending metal. However, had metallic ions been carried from one metal to the other as a result of electrical effects, we would expect to see reactions about both implants. In only one femur (cat 4, Fig. 2) which received titanium and copper, was the reaction so extensive that it spread far enough to make uncertain which one of the pair was the offending metal. Comparing this femur with the

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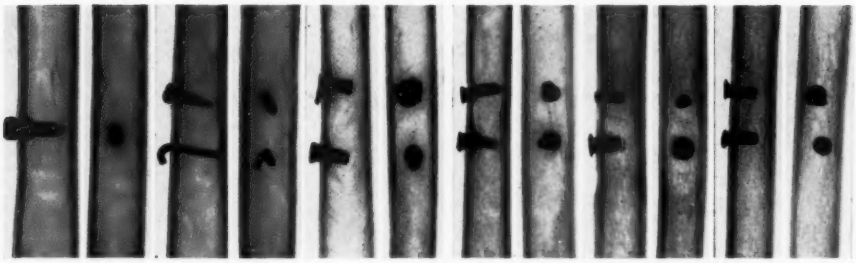
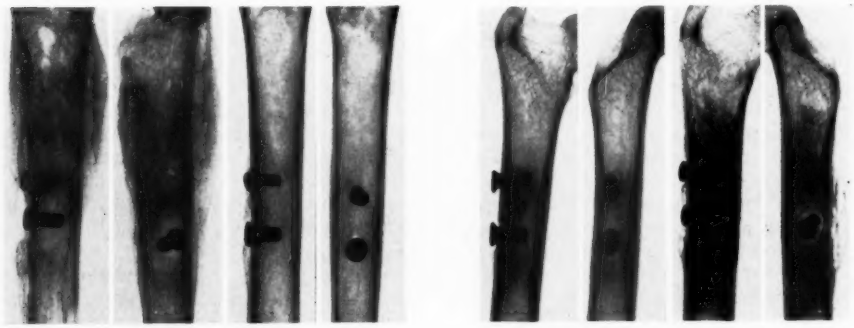
Fig. 1.



Animal 1. Animal 2. Animal 3.

Rt.	Lt.	Rt.	Lt.	Rt.	Lt.
Ti only	Ti, Pt	Pb, Ti	Au-Pt, Ti	St S, Cd	Ag, St S

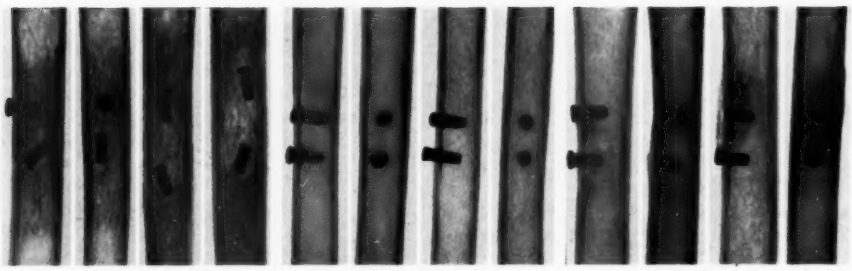
Fig. 2.



Animal 4. Animal 5.

Rt.	Lt.	Rt.	Lt.
Ti, Cu	Ti, Ag	Vit, Ag	Vit, Cu

Fig. 3.



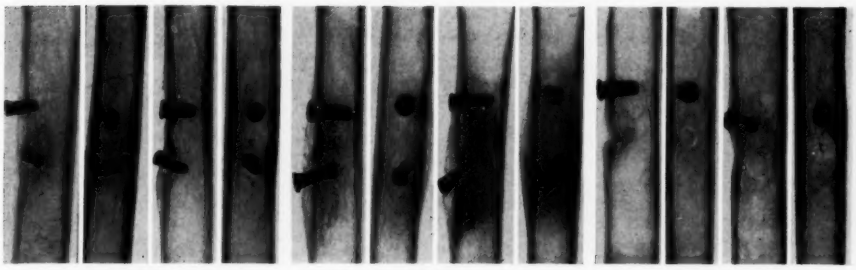
Animal 6. Animal 7. Animal 8.

Rt.	Lt.	Rt.	Lt.	Rt.	Lt.
Vit, Mn	Mn, Mn	Vit, Ti	Ti, Ti	Ti, Cd	Mn, St S

left one, makes it evident that copper and not titanium is toxic, since titanium was not reactive when paired with silver, or when used alone (cats 1 and 7). In the left femur of cat 5, the difference in potential between copper and vitallium was zero, yet a vigorous reaction occurred. From other potential measurements it can be deduced that the difference between copper and titanium is not over 20 millivolts and would not be enough to account for the extensive reaction of the right femur of cat 4.

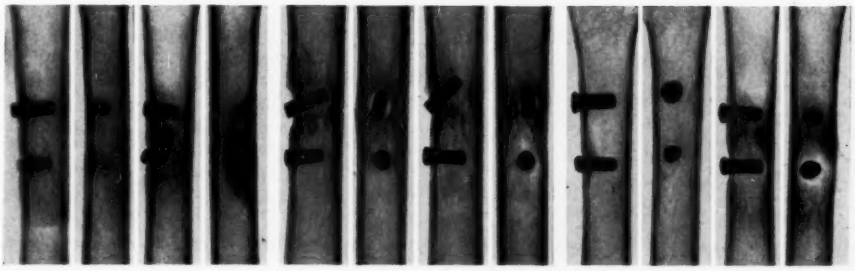
Another example of an unfavorable reaction with low potentials is seen in the case of nickel implants of cat 13, Figure 5. The potential difference between nickel and chromium on the right side was 20 millivolts, whereas on the left

Fig. 4.



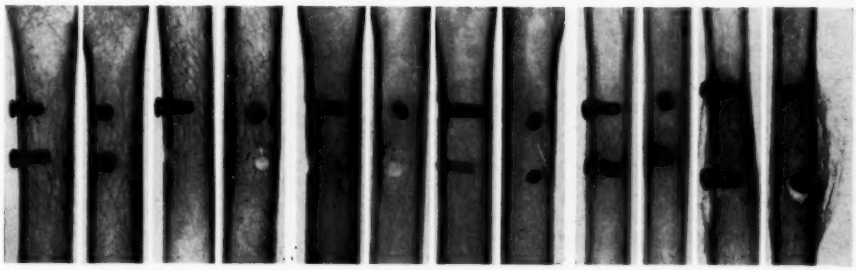
Animal 9.		Animal 10.		Animal 11.	
Rt.	Lt.	Rt.	Lt.	Rt.	Lt.
Ti, Mn	Ag, Mn	Vit, Mn	St S, Mn	Ti, Mg	Pb, Mn*

Fig. 5.



Animal 12.		Animal 13.		Animal 14.	
Rt.	Lt.	Rt.	Lt.	Rt.	Lt.
Mo, Al	Mo, Mn-Ti	Ni, Cr	Ni, Co	W, Fe-Ti	W, Co

Fig. 6.



Animal 15.		Animal 16.		Animal 17.	
Rt.	Lt	Rt.	Lt.	Rt.	Lt.
Cr-Mn, W	Ti, Be†	Mo, Be†	Mo, Al	Cr, Cr-Mn	Fe-Ti, Mn-Ti

Figs. 1 to 6. Roentgenographic positive prints of cat femurs cleaned and photographed after a postoperative survival period of 186 to 329 days. Side and end views of the metallic implants are shown in the right and left femur. The proximal end of the bones is at the top of the figures, and the metals used are listed from proximal to distal.

*This implant had sloughed out of the bone and was encapsulated in the adjacent soft tissue.

†Beryllium (atomic weight 9.02) is more transparent to x-rays than is bone. Both of these implants are *in situ*.

between nickel and cobalt it was 130. The reaction is essentially the same on both sides and is characterized by a marked erosion without cortical proliferation. Chromium has remained inert on the right while cobalt has caused some erosion on the left.

An example of moderate potential difference between lead and titanium with little reaction is seen in the right femur of cat 12 with an electromotive force of 260 millivolts. There is evidence of only a slight cortical reaction with bone grown over about half of the exposed surface of the lead im-

TABLE I.—DATA ON REACTIONS OF FEMURS OF CATS TO PAIRS OF METALLIC IMPLANTS

Cat no. and post-operative period (days)	Side and metals implanted	E. M. F. between metals (mv.)	Type of reaction
1 320	Rt. Ti only		Slight cortical thickening
	Lt. Ti, Pt	70	Slight cortical thickening
2 217	Rt. Pb, Ti	260	Cortical thickening
	Lt. Au-Pt, Ti	0	Slight surface erosion about the Au-Pt alloy
3 203	Rt. St S, Cd	400	Medullary rarefaction about Cd; St S, none
	Lt. Ag, St S	190	Slight increase of medullary density, Ag
4 217	Rt. Ti, Cu	Ti covered, 20 or less*	Abundant callus with local erosion about Cu
	Lt. Ti, Ag	Not taken	Some callus about Ag
5 210	Rt. Vit, Ag	70	Increased density, Ag
	Lt. Vit, Cu	0	Callus and local erosion, Cu
6 210	Rt. Vit, Mn	Mn is in medullary cavity	Increased density
	Lt. Mn, Mn		Cortex is healed
7 203	Rt. Vit, Ti	0	Slight cortical thickening
	Lt. Ti, Ti	0	Slight cortical thickening
8 196	Rt. Ti, Cd	400+	Medullary rarefaction, Cd
	Lt. Mn, St S	Mn is covered 400 or more*	Callus and slight local erosion about Mn
9 266	Rt. Ti, Mn	Mn is covered	Callus, and increased medullary density, Mn
	Lt. Ag, Mn	400+	Ag; erosion predominates Mn; proliferation predominates
10 259	Rt. Vit, Mn	400+	Marked proliferation about Mn
	Lt. St S, Mn	400+	
11 203	Rt. Ti, Mg	400+	Mg; not all absorbed, slight increase in density
	Lt. Pb, Mn	Mn sloughed out of bone	Pb is partly covered
12 196	Rt. Mo, Al	400+	Cortical thickening about both
	Lt. Mo, Mn-Ti	Not taken	Mo is covered by callus provoked by Mn-Ti alloy
13 186	Rt. Ni, Cr	20	Ni; marked erosion without cortical proliferation
	Lt. Ni, Co	130	Ni shows some medullary thickening; Co, rarefaction with cortical thinning
14 186	Rt. W, Fe-Ti	70	W, negative. Fe-Ti cortical thickening
	Lt. W, Co	70	Co shows local rarefaction with thickening several mm. distant
15 217	Rt. Cr-Mn, W	400+	Cr-Mn, slight cortical change
	Lt. Ti, Be	380	Practically no reaction
16 224	Rt. Mo, Be	400+	Slight cortical thickening
	Lt. Mo, Al	400+	Slight cortical thickening
17 224	Rt. Cr, Cr-Mn	400+	Some cortical and a slight medullary reaction, Cr-Mn
	Lt. Fe-Ti, Mn-Ti	Not taken	Mn-Ti has caused a vigorous reaction and is buried in callus

*Estimated from other determinations on similar couples.

plant. On the left side of the same cat the difference between titanium and a gold-platinum alloy was zero and there is practically no bone reaction, but the alloy pin remained loose as if the bone were avoiding it. This is in contrast with the growing into contact with the lead.

Another instructive example of the lack of direct correlation between potential and reaction comes from the comparison of the reactions of manganese and cadmium. When either of these was implanted adjacent to a nonreactive pin of vitallium, stainless steel, or titanium, a high potential difference resulted. Couples containing manganese gave vigorous reactions but those con-

TABLE II.—POTENTIALS AND TYPES OF REACTION OF BONE TO METALS

Potentials			Reactions		
380 mv. or more	380 to 100 mv.	100 mv. or less	Marked	Moderate	Slight
Al	Ag	Cu	(Erosion)	Ag	Al
Be	Co	Ni	Co	Cd	Be
Cd	Cr	Pt	Ni	Mg	Cr
Mg	Mo	St S	(Proliferation)		Mo
Mn	Pb	Ti			Pb
		Vit	Cu		Pt
		W	Mn		St S
					Ti
					Vit
					W

Correlation of potentials and reactions: High potential and marked reaction, Mn; medium potential and moderate reaction, Ag; low potential and slight reaction, Pt, St S, Ti, Vit, W; not correlating with the schema above, Al, Be, Cd, Co, Cr, Cu, Mg, Mo, Ni, and Pb.

A copper electrode in adjacent muscle was used arbitrarily as a zero point of reference because most of the couples in the bone contained one implant which gave a very low potential with copper. Reactions were classified according to gross appearance and x-ray photographs.

taining cadmium gave very mild ones (cats 3, 6, 8, 9, and 10), and the reactions are centered around the reactive metal and not around the pair forming the electrolytic couple. Beryllium couples with high potentials (cats 15 and 16) show even less reaction than those containing cadmium.

In one instance (cat 6) manganese implants became completely intramedullary, and the cortex healed over them. The titanium pin on the right side remained in place. One may imagine that the formation of insoluble manganese soaps from fat in marrow cavity on surface of the pins tended to inactivate them and permitted healing of cortex.

The activity of manganese was greatly reduced when alloyed with chromium (manganese, 70; chromium, 30 parts) but the potential between the alloy and a copper electrode in adjacent muscle was similar to the unalloyed manganese. A manganese-titanium alloy (manganese 65, titanium 35 parts), on the other hand, reacted similarly to unalloyed manganese. This illustrates the well known property of chromium to suppress corrosion of metals with which it is alloyed.

The present study together with the observations made on the preceding series, throws some light on the behavior of bone toward metals as determined by their solubility. Evaluation of every metal individually is necessary; for example, magnesium is very soluble but not particularly toxic, while copper is much less soluble but highly toxic. Chromium would be very toxic if it were soluble, since chromium salts are very toxic to all living tissues, but the metal caused no reaction. Beryllium caused little reaction presumably by reason of its insolubility, but beryllium salts are known to cause bone lesions similar to rickets when taken by mouth. Lead shows no toxicity as judged by the tendency of the cortex to cover it, yet lead salts are toxic.

Tantalum was not used in this series, but the report of Burke indicates that this metal is quite inert in both bone and soft tissues and has ideal physical properties. The fact that tungsten was inert in our experiments and that it is closely related to tantalum in the atomic series of the elements is of some academic interest.

PRACTICAL CONSIDERATIONS

The possibility of using powdered, sterilized metallic manganese to stimulate callus formation in nonunion of fractures is suggested by the way bone reacts to this metal. It appears to be largely inactivated in the medullary fat, as shown by the femurs in which it became intramedullary and the cortex healed over it with scarcely a trace of the original holes. The powdered or finely granulated metal might be sprinkled on the exposed nonunited ends of a bone during an open operation, or it is conceivable that it could be injected without an operation in a suspension of an absorbable medium.

Differences of electrical potentials in themselves do not cause unfavorable bone reaction, hence it seems reasonable to conclude that any alloy which might be made of metals with which bone reacted favorably individually, would be tolerated well as an alloy. This postulate should be of value to the metallurgist interested in the manufacture of prosthetic materials.

SUMMARY AND CONCLUSIONS

Two implants of dissimilar metals were paired in such a way that varying degrees of electrical potential were obtained, and allowed to remain 6 to 11 months in femurs of cats. Bone reactions were not closely correlated with the magnitude of potential differences, but remained characteristic for a given metal or alloy. Electrolysis is not the primary cause of unfavorable bone reactions. The primary causes are determined by physical and chemical properties of the metal itself. Solubility and the degree of toxicity of the dissolution products appear to be the chief factors. If electrical potentials play no part in inciting reaction it seems safe to assume that the unfavorable reactions seen in alloys are due to the presence of toxic metals (such as nickel, copper, or manganese) in them. Alloys which consist of nontoxic metals should be nontoxic regardless of potential differences of their components. Theoretically, vitallium comes nearer to meeting this requirement than stainless steel, but tantalum may prove to be the metal of choice when sufficient data on it have been accumulated.

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THE MANAGEMENT OF ACUTE EMBOLIC OCCLUSION OF THE ARTERIES TO THE EXTREMITIES

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WHEN an artery in an extremity becomes acutely obstructed by an embolus, a two-fold therapeutic problem presents itself. The first is in the nature of an emergency. It is the necessity of immediately restoring sufficient circulation to preserve the viability of the limb. The second is predicated on the successful accomplishment of the first. It is to promote therapeutically the growth of a collateral circulation so that the functional capacity of the limb as well as its viability will be preserved. Both are accomplished by increasing the volume rate of blood flow through the available collateral circulation.

For practical therapeutic purposes, any method designed to augment the quantity of blood flowing through a collateral arterial network must exert its effect by diminishing the peripheral resistance to blood flow through a dilatation of the arteriolar-capillary bed into which the collateral vessels ultimately empty. Since ischemic tissue is saturated with vasodilating substances, it should be expected that such an increase in the flow of blood through collateral channels would automatically follow the acute occlusion of a principal artery. As a matter of fact, cases of acute embolic occlusion are not infrequently seen which open and develop an effective collateral circulation without any therapeutic assistance. Many more would respond in a similar manner were it not for the fact that when an embolus suddenly occludes a peripheral artery, the arterial bed in that extremity and sometimes in the opposite extremity as well is thrown into a greater or lesser degree of spasm. I have seen instances in which a minute embolus lodged in the periphery of a leg has given rise to bilateral vasospasm of such magnitude that an organic occlusion of the bifurcation of the abdominal aorta was simulated. A case in point follows:

V. K., a white female aged 37 years, came under observation December 1, 1940. For years she had suffered from rheumatic carditis, and at the time was being treated for auricular fibrillation with failure. One hour before, she had been seized with an acute severe pain in her left leg and foot accompanied by sensations of coldness and numbness.

From The Peripheral Vascular Clinics, Cleveland City and Mount Sinai Hospitals; and from The Department of Surgery, School of Medicine, Western Reserve University.

About 30 minutes later, similar symptoms appeared in the right foot and leg.

The patient appeared to be acutely ill and in considerable distress. Her pulse was grossly irregular. Both lower extremities distal to the knees were very cold to the touch. The right foot was markedly cyanotic. Both feet exhibited a wax like pallor on elevation. No pulsation was palpable in either femoral, popliteal, posterior tibial, or dorsalis pedis arteries. The entire picture resembled that of a block in the region of the bifurcation of the abdominal aorta. However, the possibility of a minor embolus with a major degree of reflex vasospasm could not be readily ruled out; and, in view of her poor general condition, it was decided to employ conservative therapy. Within 72 hours, normal arterial pulsation had returned throughout the entire right lower extremity; and within 2 weeks, excellent pulsation was palpable in the left femoral and popliteal arteries. At this time both feet were warm and of normal color. Symptoms had disappeared. Figure 1 presents a series of oscillometric tracings illustrating this remarkable degree of bilateral reflex vasospasm resulting from a minor embolic occlusion of an artery in the distal portion of a single extremity. Patient made an excellent recovery only to expire several months later from a cerebral embolus.

The vasospasm just described has important implications concerning treatment. As has been demonstrated, an embolus lodged in the distal portion of an extremity may reflexly render the more proximal and larger arteries pulseless. Unless the possibility of spasm is considered, these larger spastic vessels may be surgically explored for the purpose of removing what is erroneously considered to be the offending embolus.

I. A., a white female aged 36 years, came under observation April 18, 1940. She had suffered from rheumatic carditis with fibrillation for many years, but was well controlled. While convalescing from an elbow operation, she suddenly experienced an acute severe pain in her right leg and foot accompanied by sensations of coldness and numbness.

The right foot and lower leg were mottled, very cold to the touch, and exhibited a wax-like pallor on elevation. Excellent pulsation was palpable in the right femoral artery; no pulsation was palpable in the popliteal artery or its branches. Oscillometric readings at the level of the popliteal space were zero. A diagnosis of an embolic occlusion of the right popliteal artery was made. Under local anesthesia, the popliteal artery was exposed. It was markedly constricted, its diameter measuring only 1/8 of an inch. The constricted vessel exhibited extremely faint pulsation and contained no thrombus. No attempt was made to explore the artery. The wound was closed and conservative therapy was instituted. Within 24 hours, the foot was pink and warm and symptoms had subsided. She made an excellent anatomical and functional recovery, and has remained well.

Another important bearing on treatment concerns the use of heat. It has been demonstrated (1, 2, 5) that external heat stimulates the metabolic activity of ischemic tissue and hastens the onset of gangrene. Therefore, when the collateral circulation in an extremity rendered acutely ischemic is so spastic it cannot relax in response to the huge concentration of vasodilating substances surrounding it, the use of heat as an additional dilating stimulus is, under the circumstances, not only illogical but dangerous.

During the acute stage of an embolic occlusion, therapy should concern itself with relaxing spastic vessels and preventing their thrombosis. To secure the desired relaxation, intravenous injections of papaverine hydrochloride in ½ grain doses every 4 hours for 48 hours and then 3 times a day for a week are almost specific (4). To prevent thrombosis of the collateral circulation pending its dilatation, and to prevent spreading thrombus formation starting at the site of the actual organic occlusion, heparin is administered (3, 6, 7, 8, 9, 10). Since many of these patients are cardiacs, heparin can rarely be administered in a continuous intravenous infusion of saline as is the usual procedure. Instead, it must be given intravenously in 4 hour doses of 50 milligrams each. This dosage may have to be adjusted to keep the blood clotting time at a minimum level of 15 minutes.

The limb is swathed in cotton and protected with an unlighted cradle. After spasm has disappeared, as indicated by an increase in the surface temperature of the foot, an improvement in its color, and subsidence of symptoms, measures may be instituted for the purpose of further stimulating the flow of blood through collateral channels. Mild local heat, the rhythmic venous occlusion machine, and the suction-pressure boot may now be safely employed.

Should the ischemia fail to improve or become progressively severe despite the administration of papaverin and heparin, an actual organic block of a major vessel must be considered and an embolectomy with the patient still heparinized performed.

Individuals who have sustained an embolic occlusion may present themselves for treatment several weeks after the acute vascular accident has occurred. In such instances, it is often found that a periarteritis involving the thrombosed vessel is stimulating afferent sympathetic neurones with resultant pain or reflex spasm of the collateral bed. Resection of the offending thrombosed arterial segment is indicated. The following cases are illustrative.

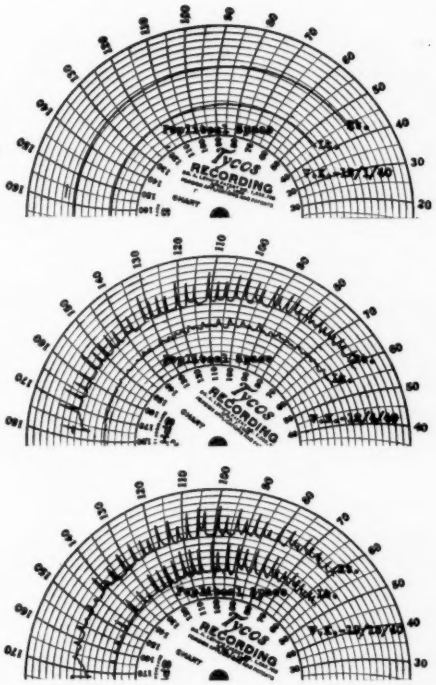

Fig. 1. A series of tracings taken with a recording oscillometer depicting the remarkable degree of bilateral vasospasm which may result from an embolic occlusion of an artery in the distal portion of a single extremity. Tracing taken December 1, 1940, 1 hour following embolic occlusion of artery in distal portion of left leg, reveals absence of pulsation in each popliteal space. Tracing taken December 4, 1940, 72 hours following acute vascular accident, reveals excellent pulsation in right popliteal space and slight pulsation in left popliteal space. Tracing taken December 15, 1940, 2 weeks following occlusion, reveals excellent and equal pulsation in each popliteal space. Conservative treatment employed throughout. Note irregularity in magnitude and spacing of pulsation due to auricular fibrillation.

M. B., a white male aged 48 years, came under observation March 27, 1939. He had suffered from rheumatic heart disease for many years and was subject to bouts of fibrillation. About 10 days before I saw him, he experienced sudden severe pain in both feet accompanied by sensations of coldness and numbness. Since then, he had been incapacitated by a peculiar type of pain referred to the calves of his legs. The pain was present constantly and was worse at night. He described the pain as squeezing; as if the calves of his legs were caught in a closing vise. The pain was so severe that morphine gave only transient relief. He also suffered from pain, coldness, and numbness of the feet but to a lesser degree.

Both feet were cold to the touch, somewhat cyanotic, and exhibited pallor on elevation. There was no tissue necrosis. Excellent pulsation could be felt in each common femoral artery down to its bifurcation. No pulsation could be detected either manually or with the oscillometer distal

Fig. 2, left. Low power magnification of microscopic section of segment of thrombosed superficial femoral artery and adherent femoral vein resected 2 weeks after acute embolic occlusion. Sections show striking changes in femoral artery, and complete occlusion of lumen by a thrombus mass composed in great part of red blood cells and fibrin. The intima in places is thickened and shows degenerative changes. The media likewise show degenerative changes. The adventitia and regional tissues show moderate to considerable round cell infiltration and some edema. The veins in the section show some thickening of the walls and some round cell infiltration and edema of the outer coats and regional tissues. A small nerve in this section shows some edema and round cell infiltration especially perineural. Diagnosis: Femoral artery occluded by recent thrombus with regional cellulitis. Thickened femoral veins with regional cellulitis. Perineural cellulitis.

Fig. 3. Low power magnification of microscopic section of thrombosed brachial artery resected 2 weeks after acute embolic occlusion. Section shows the wall of the artery to be somewhat thickened. Most of the thickening is due to a reaction in the serosa. The lumen is filled with blood that has undergone considerable autolysis. Intermingled with the blood are fibrin strands. There is a moderate amount of fibroblastic activity between the clot and the vessel wall. The adventitial coat is considerably thickened and there is noted fibroblastic activity. There is also present a moderate amount of regional round cell infiltration. Diagnosis: Organizing embolus to brachial artery with subacute periarteritis.

to these points. The calf muscles were relaxed and flabby. The symptoms in the feet were interpreted as being of ischemic origin; while the pain in the calves suggested stimulation of intravascular and perivascular sympathetic nerve fibres. Accordingly, under local infiltration anesthesia, the proximal portion of each superficial femoral artery was exposed for the purpose of performing an adventitial stripping. However, this proved to be impossible because of inflammatory adhesions between the thrombosed arteries and the adjacent femoral veins. The arteries were opened and the thrombi found to be adherent. A 2 inch section of each thrombosed artery and adherent vein was excised (Fig. 2). The operation gave immediate and complete relief of the pain in the calves of his legs. Subsequently, measures were instituted to stimulate the growth of a collateral circulation. He recovered complete use of his extremities and has been well since.

P. D., a white male, aged 22 years, came under observation February 12, 1941. About 2 weeks before admission he experienced a sudden severe pain in the antecubital space of his right arm. The pain rapidly spread up the inner aspect of his right arm, and the hand became cold and numb and began to ache. The pain, coldness, and numbness in hand became increasingly severe, the end of the thumb and forefinger became black, and ability to move the fingers was lost.

Medical consultation revealed the presence of an aortic valvulitis with questionable congenital heart disease. X-ray was negative for cervical ribs. The right hand was ice cold, sweaty, cyanotic, and assumed a wax-like pallor on elevation. Cutaneous sensibility was absent, and the patient was unable to move his fingers. The distal phalanges of the first and second fingers were gangrenous. The radial and ulnar arteries were pulseless. Oscillometric readings at the level of the right forearm were zero. The entire length of the brachial artery from its junction with the axillary down to its bifurcation was palpable as a pulseless tender cord-like structure. It was felt that this thrombosed vessel was giving rise to a reflex spasm of the collateral circulation to the hand. Accordingly, under general anesthesia, the entire length of the brachial artery was exposed. It was completely thrombosed. The artery was opened, and the thrombus was found to be adherent. Feeble pulsation was present in the terminal portion of the axillary artery. The thrombosed brachial artery was severed at its junction with the feebly pulsating axillary. Within a minute, the ligated stump of the axillary artery dilated and began to pulsate vigorously. The entire length of the thrombosed brachial artery was excised (Fig. 3). Twenty-eight hours later, the patient was able to move his fingers, sensibility had returned, the hand was pink and warm, and symptoms had

disappeared. About 3 weeks after operation, he suffered a right cerebral embolus with complete left hemiplegia. He survived this episode and is still living. The hemiplegia has remained. Fortunately, adequate function has been restored to the right hand, thus sparing the boy from total incapacitation.

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GASTROSTOMY—JEJUNAL INTUBATION

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GASTRIC surgery is still attended by primary mortality and morbidity which is not commensurate with the magnitude of the operations. Hospital mortality rates vary from 10 to 20 per cent as shown in recent reports from representative clinics. From the evidence which is constantly accumulating, it is becoming more and more apparent that much of this excessive mortality is the result of malnutrition which is present to a minor degree in all and to a severe degree in many of the patients subjected to gastric operations. Only recently has there developed an appreciation of the extent of this depletion of such vital nutritional elements as plasma proteins and vitamins and the far reaching influence of these deficiencies upon the repair of tissues, upon gastric and intestinal motility, and upon the distribution of fluids.

In autopsy reports many of the deaths are attributed to the pathological findings which are immediately apparent but which in reality are often secondary to nutritional deficiencies. For example, when a patient who has depleted his food stores by starvation resulting from pyloric obstruction dies following operation, the autopsy may reveal such obvious causes of death as pulmonary edema, or as peritonitis resulting from leakage from the line of suture. In all probability, however, the edema resulted from hypoproteinemia or the leakage from the failure of tissue repair caused by protein, vitamin C, and possibly other unknown deficiencies.

In most of these malnourished patients it is impossible to replenish their depleted food stores before operation is undertaken and one can at best provide only a very temporary supply of certain essential elements. To this end, however, all available facilities for rehabilitation, such as the liberal administration of water, sugar, whole blood, blood plasma and vitamins, should be utilized. Since the nutritional demands are tremendously increased following operation and since the parenteral route meets these demands so inadequately, it is very important to provide nourishment as soon as possible by alimentation. This can be done starting immediately following operation by means of oral jejunal feedings. Following Ravdin's report approximately 3 years ago, the method with technical variations has been used by me almost routinely. In the earlier cases two Levine tubes were threaded into the stomach, one through each nostril before the operation was started. At the completion of the gastrojejunal anastomosis one of these tubes was threaded through the stoma into the distal loop of the jejunum for a distance of 8 to 12 inches. Through this tube feedings were administered every hour, starting as soon as the patient returned from the operating room. Each feeding consists of 2 to 4 ounces of peptinized skimmed milk containing 5 grams of glucose to each 100 cubic centimeters of the mixture, followed in some instances by 1 or 2 ounces of normal salt solution, as indicated, to maintain fluid balance. By this means alone the patient receives from 2800 cubic centimeters of fluids to as large quantities as desired in addition to the normal salt requirements, so that it is unnecessary to administer fluids parenterally. In addition these feedings provide in 24 hours 150 grams of glucose, an equal quantity of milk sugar, 95 grams of the much needed protein, and the minimal caloric requirement of 1,795 calories. To these feedings there has been added the vitamins B-complex and C in the quantities indicated, and other medications as desired. Because 2 patients pulled

Fig. 1. Oral-jejunal intubation for feeding. Three days after an anterior Pólya resection showing the two Levine tubes which were threaded into the stomach (one through each nostril) before operation. At operation one tube was threaded through the stoma, *S*, into the distal loop of the jejunum, the other one was left in the gastric stump in order to keep it empty by constant suction. The area of increased density between *O* and *S* represents the thick edematous walls of the stomach and jejunum around the stoma.

Fig. 2. Gastrostomy-jejunal intubation for feeding. Roentgenograms taken 7 days after a gastroenterostomy to relieve pyloric obstruction due to postcholecystectomy cicatrization about the duodenum. The tube enters the abdomen at *A*, the stomach at *B*, and the jejunum through the stoma at *S*. Note the area of decreased density outlining the enormously dilated stomach. A small amount of barium taken by mouth outlines the cardia while some barium injected through jejunal tube can be seen in jejunum. Incidentally, shadows of two right renal calculi are shown.

out the Levine tubes unintentionally during sleep the original procedure has been modified in the malnourished patients as shown in the roentgenogram, Figure 1.

After the gastrojejunal anastomosis is completed a catheter gastrostomy is done, and the tip of a catheter is threaded through the stoma into the distal segment of the jejunum. The wall of the stomach at the site of gastrostomy is anchored to the abdominal wall and the proximal end of the catheter is brought out through a stab wound to the left of the incision. It has been learned that the catheter can be passed most simply through the stoma into the jejunum by grasping the tip of the catheter in a curved hemostat with which it is directed through the small gastrostomy incision into the jejunum. Through this catheter feedings are administered as has previously been described.

If the jejunum is distended rapidly some discomfort may be produced. Therefore, the feedings are administered slowly drop by drop from a gravity bottle. The stomach is kept empty by constant suction applied through the Levine tube in the stomach.

Two ounces of water are given by mouth every hour. This serves two purposes. It pleases the patient and, as it returns through the Levine tube, it washes the stomach and the tube. On the third day suction is discontinued, but the tube is left in place so that suction can be resumed in case of distress or other evidence that the stomach has failed to empty. On the fourth day hourly feedings of 2 ounces of milk and cream in addition to water are given by mouth and the jejunal feedings are reduced to 2 ounces. On the 5th day a 6 meal bland gastric diet is started and jejunal feedings are discontinued. If oral feeding progresses satisfactorily the gastrostomy catheter is removed on the 7th or 8th day.

This method of intubing the jejunum has certain advantages over jejunostomy. It does not fix the jejunum to the abdominal wall or cause other adhesions about it to act as potential sources of

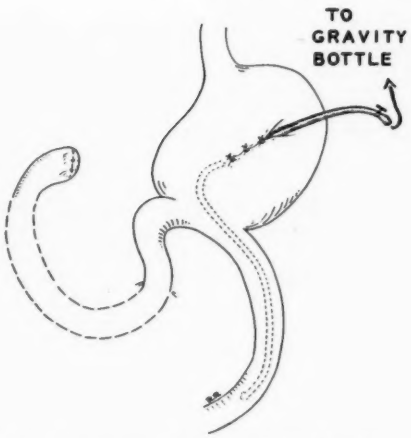

Fig. 3. Gastrostomy-jejunal intubation supplementing gastric resection.

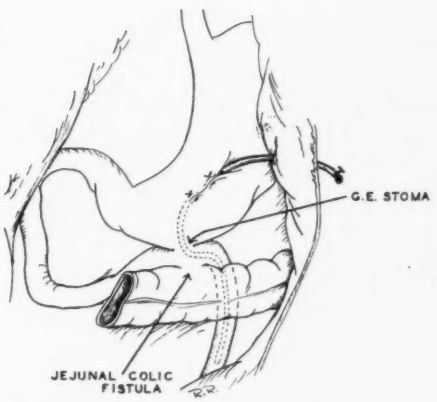

Fig. 4. Gastrostomy-jejunal intubation for preliminary jejunal feeding of patients with gastrojejunocolic fistula. The tube by-passes the jejunal-colic fistula and delivers food and water where it will be assimilated. After adequate restoration of nutrition the radical corrective operation can be done with much less risk.

jejunal obstruction and there is less likelihood of leakage.

In our small series of cases no complications or ill effects have been encountered. To the contrary, convalescence in each case has been extraordinarily uneventful.

It is obvious that in cases with small residual gastric pouches which retract up under the costal margin, the procedure is technically impossible. In these cases recourse is had to oral jejunal feedings through the Levine tube which had been passed into the stomach before operation. Fortunately, however, little difficulty has been encountered in the severely malnourished patients who are most in need of immediate feeding because they are thin and lax from much loss of weight and their stomachs are usually large as a result of obstruction.

Recently, jejunal feedings by means of gastrostomy-jejunal intubation have been used to rehabilitate a severely depleted patient with a gastrojejunocolic fistula. A diagram of the procedure is shown in Figure 2. The rapidity of both physical and biochemical restoration was impressive as was the convalescence from the corrective operation which was done 12 days later. Following this corrective operation which included partial resection of the stomach, the gastrostomy tube was threaded into the jejunum through the new stoma and the jejunal feedings were continued.

MULTIPLE MYELOMA

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IN a previous communication, two of us (Ghormley and Pollock) reviewed the clinical and laboratory findings in 86 cases of multiple myeloma encountered at the Mayo Clinic between January 1, 1924, and December 31, 1936. This present study was undertaken in an endeavor to bring the statistical survey of this disease up to date. Forty-one additional patients who had multiple myeloma were examined in the last 3 years, making a total of 127 patients examined and treated in the 16 years from January 1, 1924, to December 31, 1939. It is of interest to note the increase in the number of cases in which a diagnosis of multiple myeloma has been made since our paper on this subject was published.

Multiple myeloma is a highly malignant tumor of the bone marrow which tends to occur after the fifth decade of life. Although the disease generally is insidious in its onset, on occasion it may run a fulminating course. In one of our cases only 4 months elapsed from the appearance of the first symptom until the death of the patient.

The etiology is unknown. Men are affected about twice as frequently as women. Trauma does not appear to influence the onset of the disease; although in several cases history of injury was elicited on inquiry, its importance as an etiological factor was not emphasized by the patients. The original description made by Dalrymple in 1846 of the pathological findings cannot be improved. Speaking of the appearance of two vertebrae and a rib at necropsy, he said: "the disease appears to have commenced in the cancellated structure of the bone for the external osseous laminae are firmer and more healthy than the internal. . . ." and again, "the smoother surface of the rib, however, is raised by internal growths elevating the outer laminae here and there into irregularly sized and rounded dark red projections visible through the periosteal covering. The outer layers are steel hard requiring the exertion of some force to cut them; they are thin, however, and, when sliced, expose large cancellous cavities filled by a red gelatiniform substance threaded here and there by fine bony fibers. It is in these fibers of still-existing bone that many of the more important morbid changes may be witnessed."

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Microscopically, the tumors are made up predominantly of cells which closely resemble plasma cells. They possess the same tinctorial characteristics, which can be brought out by the Unna-Pappenheim stain. However, the nucleoli in these cells are more prominent than those in normal plasma cells. If a tumor nodule is the source of the material examined, the histological appearance is uniform and comprised almost entirely of these cells. The myeloid tissue and fat spaces seen in normal marrow are not encountered. On the other hand, if a portion of marrow between tumor nodules is examined, the picture may be essentially normal except for the finding of isolated tumor cells or small nests of tumor cells.

Imprint preparations made from bone marrow obtained at biopsy or smears made from aspirated material, stained with any one of the Romanowsky combinations of stains, lend a somewhat different appearance to these cells. They vary in size from 7 to 30 microns and have a definite outline. They are usually oval but occasionally are somewhat irregular. The cytoplasm ordinarily is deeply basophilic and has a lighter staining zone adjacent to the nucleus. The nucleus is round or oval and has a variable type of nuclear structure, the chief characteristic of which is a large, conspicuous, sharply demarcated nucleolus. The chromatin usually is arranged either in fine or coarse strands, rarely in dense masses, and is sharply differentiated from the parachromatin. The identity of tumor cells in myeloma has not been established. Inasmuch as they differ from normal plasma cells and have a characteristic appearance morphologically, they are now usually referred to as "myeloma cells."

The progenitor of the myeloma cell is unknown. Many theories have been advanced and the cells which have been suggested as possible sources of these elements are as follows: myeloblasts; dysplastic hemocytoblasts; the reticuloendothelial cells; lymphocytes; megakaryoblasts and osteoblasts. From evidence in recent literature and in our material, it seems likely that in most instances the myeloma cell is derived from reticuloendothelium.

SYMPTOMS

The symptoms are diverse and, frequently, apparently unrelated. There are no symptoms

which are pathognomonic of the disease. Of our entire series of 127 cases, only 32 were proved at pathological examination. Eighty-three of the patients were males and 44 were females. The oldest male was 75 years of age, the youngest 4 years. The average age of the patients at onset of symptoms was 54 years. The duration of symptoms at the time of the first examination at the clinic ranged from 3 weeks to 5 years. The average duration of symptoms was 1 year. The longest duration of the disease was 9 years, the shortest 4 months. Pathological fractures were present in 13 proved cases, 40.6 per cent.

Backache, by far the most common symptom, was the major complaint in most of our cases. When this was the sole symptom, the reason for the erroneous diagnosis of arthritis of the spinal column or neuritis is understood. Loss of strength and progressive weakness were the second most common cause for the patient's seeking advice. Anemia, loss of weight, or occurrence of a pathological fracture was described less frequently, and the presence of a palpable tumor was rare.

In about 70 per cent of our cases, albuminuria was present, although in only 36.5 per cent of cases in our second series was renal damage present, as evidenced by casts, hematuria, and an elevated value for blood urea. It is possible for a condition which has been diagnosed and treated as nephritis ultimately to be proved multiple myeloma. In one of our cases, excessive albuminuria of long standing was the only finding; on further investigation, Bence-Jones proteinuria was discovered. Results of sternal puncture, advised because of this finding, revealed the true nature of the disease as multiple myeloma. Investigation for Bence-Jones bodies was made in 112 of the 127 cases, with positive findings in 68, 60.7 per cent. A similar research in the proved group of cases of multiple myeloma gave positive findings in only 12 of the 29, 41.3 per cent. The more important of the various investigations carried out are listed in Table I.

TABLE I.—SUMMARY OF DATA CONCERNING CONSTITUENTS OF BLOOD IN ENTIRE SERIES

Investigation	Estimations*	Abnormal results		
		Type	Cases	Per cent
Albumin-globulin ratio	23	Reversed	13	56.5
Uric acid	6	Elevated	4	66.6
Blood cholesterol	5	Reduced	3	60
Blood calcium	48	Elevated	10	20.8
Blood phosphorus	42	Elevated	4	9.5
Blood phosphatase	22	Elevated	4	18.1
Serum sulfate	16	Elevated	5	31.2
Serum protein	20	Elevated	10	50
Blood urea	57	Elevated	21	36.8
Sedimentation rate	29	Elevated	23	79.3
Blood creatinine	9	Elevated	5	55.5
Bence-Jones protein in urine	112	Positive	68	60.7

*One estimation listed per case.

DIAGNOSIS

Although symptoms are not pathognomonic of this disease, the discovery at examination of several of the findings listed in Table I should suggest the possible diagnosis of multiple myeloma.

Biopsy or sternal aspiration to confirm the diagnosis of multiple myeloma is warranted in cases in which the patient is a man more than 50 years of age who has changes in bones and progressively severe backache associated with Bence-Jones proteinuria or high level of protein in the serum. Multiple, punched-out areas of destruction in the skull, ribs, and spinal column usually are accepted as roentgenological evidence of multiple myeloma, but it must be recognized that widespread metastatic carcinoma may give rise to similar appearances. In this connection, it is well to remember that the presence of myeloid immaturity and a "greasy" appearance in the blood smears described as suggestive of multiple myeloma are found in metastatic malignant disease which involves the bone marrow and also in paroxysmal hemoglobinuria. Magnus-Levy admitted the possibility of Bence-Jones proteinuria resulting from activity of normal marrow.

The condition of the patient is not always an index of the extent of the disease. We have been astonished to observe patients in comparatively good condition who had extensive skeletal destruction and again, we have been embarrassed at our inability to discover a definite skeletal focus on examination of a patient who is dying and has all other clinical signs and evidences of multiple myeloma. With so many possibilities for error, accurate diagnosis is difficult. The diagnostic results of biopsy are excellent, but many patients are reluctant to undergo a surgical procedure which is not calculated to give relief.

The comparatively recent introduction of sternal aspiration has placed at our disposal a procedure which will permit accurate diagnosis in most cases. The method is so simple in application that its routine use in suspected cases should be possible. Material is aspirated from the marrow cavity of the sternum by means of a dry syringe

and is placed in a 2 cubic centimeter paraffin lined test tube containing a small amount of heparin. Material is mixed well to prevent clotting. Smears are made from this material which are stained with Wright's stain and then by Giemsa's. The presence of myeloma cells is diagnostic of the condition but their absence does not rule it out.

PROGNOSIS

Prognosis is uniformly poor in all cases in which evidence of involvement of bone is present. In our entire series, the average duration of life after diagnosis had been made was a year, which conforms fairly accurately to the figure of 14.05 months which we gave originally in our proved series. The longest duration of the disease in our proved group of cases was 9 years and 2 months, and the shortest, 4 months.

In cases in which multiple myeloma affects the soft tissues only, it is possible that complete extirpation of the lesion will result in cure.

Other therapeutic measures are foredoomed to failure, yet there is evidence from the follow-up reports of our patients that temporary relief and improvement have followed the use of roentgen therapy and general tonic measures. At this time the authors are unable to state whether the patients' lives have been prolonged materially by the use of these measures.

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THE SURGICAL ANATOMY OF THE SUPERIOR HYPOGASTRIC PLEXUS

With a Report of 150 Personal Dissections

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SINCE its existence was first noted by von Haller many anatomists and surgeons have studied and given varied names and descriptions to that collection of sympathetic fibers which only of late is being designated properly as the "superior hypogastric plexus." This plexus, which is rarely a single nerve and is always prelumbar, is commonly and erroneously referred to by the misleading term, "the presacral nerve" (Latarjet and Bonnet). Recently Davis (23–26), Labate (38) and others have stressed the inaccuracy of the term "presacral" and have come to popularize the more acceptable terminology of Sappey, "superior hypogastric plexus."

In 1925 Cotte introduced the operation of resection of the superior hypogastric plexus for the relief of pelvic neuralgia, vaginismus, dysmenorrhea, hypoplasia of the uterus, metrorrhagia and sexual neurosis (2–3). Subsequently the procedure was popularized and the indications for its use extended by numerous contributions, particularly those of Cotte (5–20) and of Leriche (44–46). The successful and widespread use of extirpation of the superior hypogastric plexus led to its adoption for the relief of pain arising from such varied pathological conditions as (a) inoperable carcinoma of the pelvic viscera; (b) intractable primary dysmenorrhea; (c) cord bladder; (d) intractable cystalgia; (e) spasm of the bladder neck; (f) obstipation of rectal origin; (g) Hirschsprung's disease; (h) pruritis vulvae; (i) vaginismus; (j) dyspareunia; (k) sclerocystic degeneration of the ovaries; (l) kraurosis vulvae; (m) severe persistent postoperative pelvic pain, and pelvic and abdominal pain of obscure origin.

The increase in indications for extirpation of the superior hypogastric plexus and the wide adoption of the procedure as reflected by the numerous reports in recent literature created the need for, and gave a marked stimulus to, the study of the available literature on the detailed anatomy and surgical anatomy of the plexus. This was found to contain many conflicting reports. In fact, after noting the repetition of inaccuracies contained in the older literature one is tempted to agree with Byron Robinson when he states "It would astonish any student to know how little has been published in regard to the nervous system of the female genitals that is of an original character."

The existence, in the literature, of this wide variety of descriptions of the plexus led to a series of careful studies by a number of recent investigators, but as Davis (23–26) has so well stated, "Painstaking and exhaustive though this work has been, and possibly because of these factors the variations in the findings of different writers on the morphology of the plexus are even wider than those exhibited by the older authors."

While all types of plexus patterns have been reported, the main conflict lies between those who have reported the predominance or sole existence of "presacral nerves" and those who have substantiated the finding of a predominance of "superior hypogastric plexuses." An understanding of the development of these differences can be derived from an appreciation of the fact that single nerves, bilateral cords, and a multiple variety of plexus formations occur, and when an investigator has had occasion to report a short series of dissections in which a single type predominates there is apt to be an emphasis on that type, whereas the result of a larger series would at once demonstrate that all varieties reported may occur, and that the plexus patterns predominate. It is also true that superficial and inadequate dissection will frequently reveal a single nerve or bilateral cord, whereas further careful dissection of the same subject will reveal many intercommunicating twigs and may uncover a typical plexus arrangement. It is hoped that this investigation, containing as it does the largest group of detailed dissections thus far reported, will tend to crystallize more clearly our concept of the morphology of the superior hypogastric plexus.

MATERIAL AND METHODS OF STUDY

The specimens included in this study were obtained from the routine cadaveric material in the department of gross anatomy, Tulane Univer-

From the Departments of Gross Anatomy and Gynecology, Tulane University, School of Medicine.

sity, during the summer sessions 1938 and 1939 and the regular sessions 1938–1939 and 1939–1940, which were made available by Dr. Wilbur C. Smith and also several autopsy specimens from Touro Infirmary, New Orleans, were provided through the courtesy of Dr. John A. Lanford. While 10 dissections were done on infants in order to determine whether there are differences in the morphology of the plexus in the infant and the adult, as claimed by some investigators, none was found and the infant material is not included in this report. This report considers the findings in 150 adult dissections, representing 20 females and 130 males. Of the 20 females 14 were negro and 6 white, while 96 of the male specimens were negro and 34 white. This preponderance of the negro material is in accord with the usual percentage distribution in the anatomical material obtained by this laboratory, and though there are many interesting studies on anatomical and surgical peculiarities in the negro, particularly those of Matas, Souchon, and Hoffman, there appeared to be no differences in the morphology of the superior hypogastric plexus in the two races and therefore for statistical purposes the group will be considered as a whole throughout the following discussion.

Detailed dissections of the entire abdominal and pelvic sympathetic system were made on the first 32 cadavers. This included a study of the celiac plexus, the aortic plexus, the ovarian and renal plexuses, the lumbar sympathetic trunks, and the superior hypogastric plexus. The connections of the superior hypogastric plexus, including all of its afferent and efferent fibers, with the ganglionated sympathetic trunk and the sympathetic ganglia proper were studied. The fibers were traced from their origins to their final distribution in the pelvic viscera. In the remaining subjects the detailed gross anatomy of the superior hypogastric plexus and the interiliac trigone was recorded with notations on the occurrence of anomalous structures in the interiliac trigone. In every instance a record was made of the size of the interiliac trigone and a sketch made of the morphology of the plexus and the relationships existing between the plexus and the contents of the interiliac trigone. In addition, observations were made on the variations of the sigmoid mesocolon. The female subjects, in every instance, were submitted to detailed study.

CONNECTIONS OF THE SUPERIOR HYPOGASTRIC PLEXUS

The superior hypogastric plexus is a direct downward continuation of the intermesenteric nerves of Petit-Dutaillis-Flandrin. By way of these nerves it is connected above with the celiac plexus and the lumbar sympathetic ganglia (upper 2 or 3). The intermesenteric nerves are composed of several (2 to 6) parallel fibers on either side of the aorta. These parallel fibers are connected by innumerable fibers and form the intermesenteric or aortic plexus. The intermesenteric nerves arise from the renal or aorticorenal ganglion, the periarterial plexus of the renal artery and the transverse aortic bar, and the first and second lumbar sympathetic ganglia. They at first lie on the lateral aspect of the aorta, the right being somewhat further lateral than the left, which is closely adherent to the lateral aspect of the aorta. They then pass downward and medially to the anterior surface of the aorta, on which they continue downward (receiving and distributing fibers to the inferior mesenteric ganglion and plexus) to the bifurcation of the abdominal aorta at which level they enter the interiliac trigone and terminate by forming the superior hypogastric plexus. Just prior to their termination they receive fibers from the lower lumbar ganglia.

The plexus is connected above with the inferior mesenteric periarterial plexus, and when present the inferior mesenteric ganglion. These fibers may run downward to join the plexus directly or may join the intermesenteric nerves.

The superior hypogastric plexus receives fine branches from each of the lumbar sympathetic ganglia. The contribution of the superior (first and second) ganglia is usually the more marked, frequently consisting of several distinct fibers which are contributed to the plexus via the intermesenteric nerves. The fibers from the inferior ganglia are inconstant and of finer caliber and when present are of a lesser number than the superior. The branches from the inferior lumbar ganglia occasionally join the intermesenteric nerves but more frequently enter directly into the superior hypogastric plexus, being found inferior to the termination of the intermesenteric nerves in the superior hypogastric plexus. The number of ganglia in the lumbar section of the cord varies, hence the terms superior and inferior ganglia are used in preference to numerical designations. However in every case fibers are contributed to the plexus by all the lumbar sympathetic ganglia. The preponderance of fibers from the upper lumbar ganglia is in keeping with the observations of Hovelacque, Delmas and Laux, Davis, Labate, and others.

In addition to these twigs from the lumbar sympathetic ganglia, fine fibers running from the sympathetic trunk proper to the superior hypo-

gastric plexus were demonstrable in 3 instances. The rarity of these fibers is in keeping with the finding of Davis, and contrasts with their frequency as reported by Latarjet and Bonnet. Of the 3 dissections in which these were seen, they occurred bilaterally in 2 instances and only on the left in 1 instance. All were short, fine fibers and ran almost transversely from sympathetic trunk to superior hypogastric plexus.

The fibers arising from the lumbar sympathetic ganglia proper emerge from the medial aspect of the ganglia as fine though extremely tough filaments which are usually single, though occasionally multiple. They course downward and medially posterior to the common iliac artery of that side and anterior to the vein. This relationship of artery, nerve, and vein is quite constant though in 5 dissections the nerve fibers passed posterior to both the artery and vein, and in 3 instances the fibers passed anterior to both structures. The nerves enter posteriorly at the superior aspect of the superior hypogastric plexus. In specimens in which a single "presacral nerve" occurs the fibers usually join the lateral borders of the nerve cord. In instances in which bilateral nerve cords occur, fibers join the lateral aspect of the ipsolateral nerve cord, while in the usual instance these nerves join the lateralmost portions of the plexus.

The sacral ganglia do not usually contribute fibers to the superior hypogastric plexus, though in some instances the first sacral ganglia may supply the plexus (6 per cent). Where this occurred the fibers arising from the first sacral ganglion coursed obliquely upward from the ganglion to join the plexus. In 2 instances short horizontal fibers from the first sacral ganglion joined the superior hypogastric plexus in addition to a full complement from the lumbar ganglion. The sacral ganglia usually intercommunicate via short, fine filaments which are immediately prevertebral and posterior to the fibroadipose lamina containing the fibers of the superior hypogastric plexus (41). The sacral nerves contribute many fibers to the lateral aspect of the Frankenhauser plexus.

The larger portion of the fibers of the plexus gradually diverge toward the lateral aspect of the interiliac trigone to terminate in the paired inferior hypogastric nerves. The chief innervation of the ureter is derived from these nerves. The inferior hypogastric nerves continue anteroinferiorly on the lateral pelvic wall and enter the uterosacral ligaments through which they course to the lateral aspect of the rectal ampulla, to terminate in the plexus of Frankenhauser. This rich sympathetic nerve fiber content of the uterosacral ligaments has not been sufficiently appreciated and is of considerable clinical interest since one frequently observes edematous and especially tender uterosacral ligaments associated with various types of pelvic pathology.

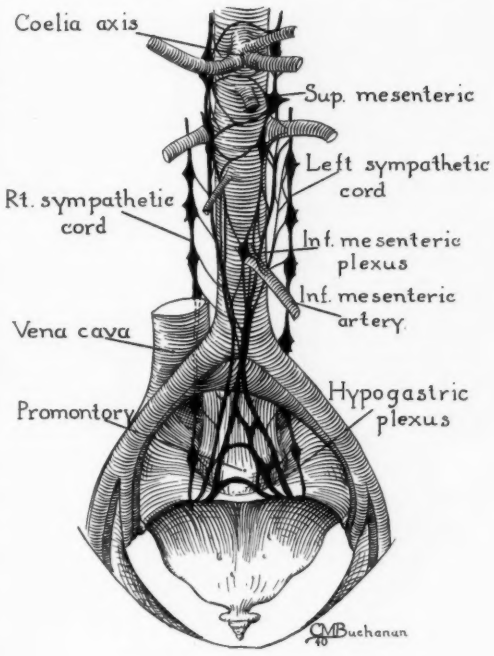
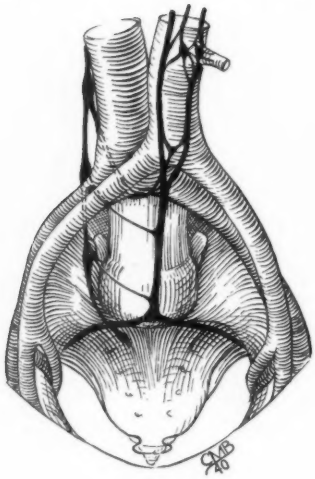


Fig. 1.

There has been considerable discussion in the literature as to the existence of the Lee-Frankenhauser ganglion or plexus. Hovelacque referred to the anterior portion of the inferior hypogastric plexus as "the so called ganglion of Frankenhauser." Lee, Frankenhauser, Robinson, Hashimoto, Jung, and Kehrer have all described the mass as a true sympathetic ganglion. It has been described as a grayish white plexus in the form of a quadrilateral mass whose limits and dimensions are not fixed, the medial surface of which is joined by the inferior hypogastric nerve. From the mesial aspect the pelvic visceral sympathetic innervation is derived, while the lateral aspect has an extensive anastomosis with the sacral nerves. Beautiful illustrations of dissections of the Frankenhauser plexus are given by Fontaine and Herrmann. The existence of this plexus, now well demonstrated anatomically, has been confirmed clinically by successful novocain and alcoholic block of the Frankenhauser plexus area which is an accepted surgical procedure.



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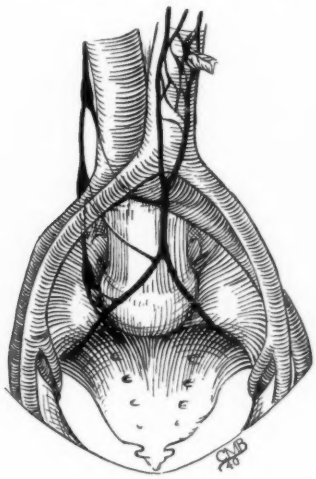

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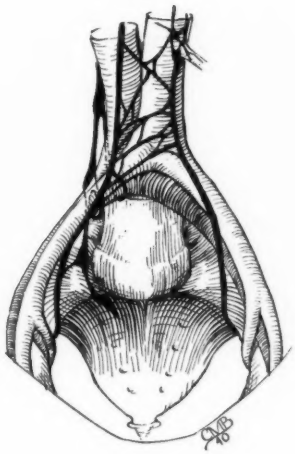

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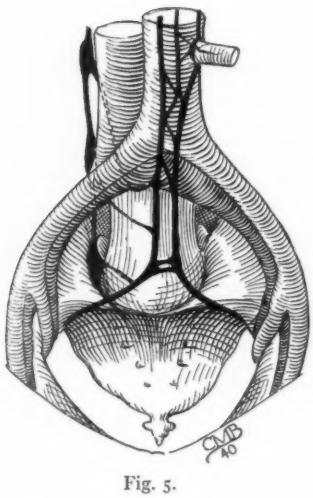

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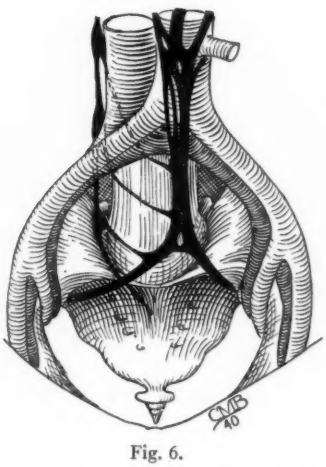

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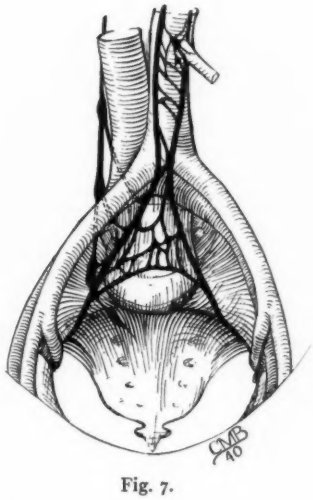


Fig. 7.

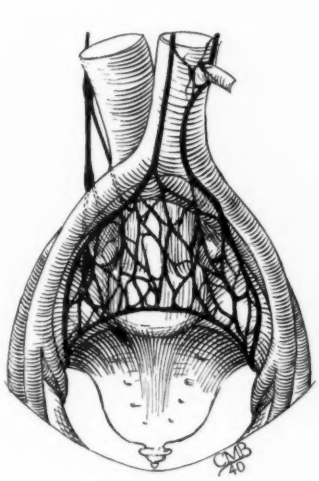
The superior hypogastric plexus also contributes filaments to the periarterial plexuses of the neighboring arteries: superior hemorrhoidal, the middle sacral, the external iliac and all the branches of the hypogastric.

The several fine filaments to the superior hemorrhoidal artery pass laterally from the superior portion of the left aspect of the superior hypogastric plexus and enter the sigmoid mesocolon. They are distributed to the sigmoid and may send fine branches to the plexus of Frankenhauser.

Infrequently fine filaments join the middle sacral periarterial plexus. This is occasionally true of fibers to the external iliac artery (demonstrable in only 7 instances). The rarity of this occurrence coincides with the report of Davis who takes issue with the report of Latarjet and Bonnet in which these fibers were discussed as though a common finding.

A diagrammatic schema of the connections of the superior hypogastric plexus is given in Figure 1.

The sensory, or afferent, fibers course in a manner which probably is similar to that of the



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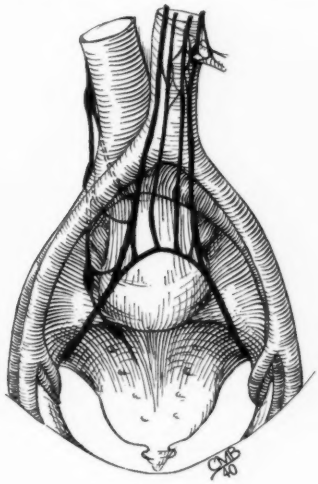

Fig. 9.

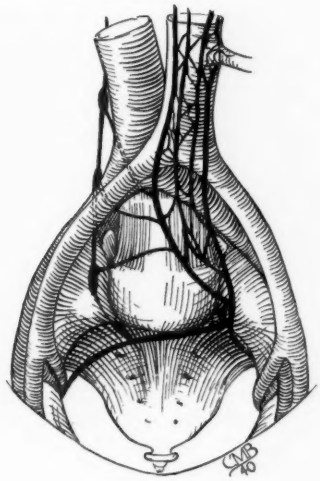

Fig. 10.

motor, or efferents, except that they go via the posterior roots to reach the nerve cells of the posterior root ganglia. The afferent fibers of all the pelvic viscera transverse the superior hypogastric plexus with the exception of the ovarian and possibly some of the fibers of the fallopian tube which according to the physiological and anatomical researches of Labate and Reynolds "have no connection by way of the superior hypogastric plexus, nor do they traverse the inferior mesenteric ganglia or the lower aortic plexus" (38). This observation is of considerable clinical importance, and is borne out by the results of sympathetic nerve block. The wider recognition of this contribution will call a halt to the needless (and of course unsuccessful) attempts to relieve pain of ovarian origin by superior hypogastric sympathectomy. The afferent nerves from the ovary are contained in the periarterial ovarian plexus and reach the tenth thoracic level of the spinal cord (Kuntz). The ovarian plexus is found in the suspensory ligament of the ovary and is joined by an external tubular branch from the fallopian tube. Five or 6 efferents of the tubular branch course through the broad ligament and reach the lateral aspect of the periarterial uterine plexus.

The uterine afferent fibers traverse the Frankenhauser and then the superior hypogastric plexuses to reach the cord at the level of the first lumbar to tenth thoracic segment (Kuntz). A detailed and excellent résumé of our current knowledge of the innervation of the uterus is given by Reynolds while a clear exposition of the innervation of the bladder may be found in McLellan's excellent monograph.

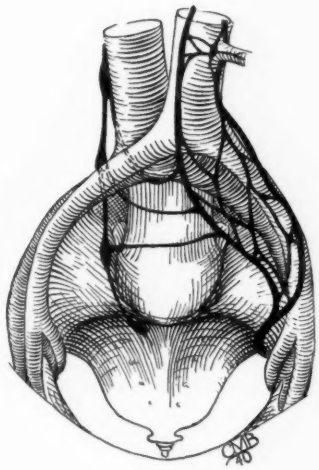

Fig. 11.

MORPHOLOGY OF THE PLEXUS

The superior hypogastric plexus is always found within the interiliac trigone, an area bounded by the bifurcation of the aorta above, the common iliac arteries laterally, and a line connecting these vessels at the promontory of the sacrum below. There is usually a plexus, uncommonly bilateral cords, and rarely a single "presacral" nerve. The plexus is triangular in shape with its apex up-

ward, representing the convergence of the intermesenteric nerves, and its base inferiorly where the main groups of nerve fibers diverge to terminate in the inferior hypogastric nerves. The position of the nerves whether as single cords or various plexus patterns is always prelumbar and never presacral.

When the intermesenteric nerves fuse at the apex of the interiliac trigone and continue without divergence until the very base of the trigone the resultant pattern is a single nerve cord, the so called presacral nerve. This is relatively uncommon, 2 per cent in this series (Fig. 2). Even this single presacral nerve pattern may be classified as a plexus, if one considers the microscopic studies of Elaut, who was able to demonstrate clearly in transverse sections of the interiliac fibroadipose layer at least 4 or 5 separate islets of nerve tissue which are lost in the fat infiltrated subperitoneal membrane and have no reciprocal connections. In 2 per cent of our dissections the intermesenteric nerves enter the trigone, slightly separated, and after continuing down for 1 to 1.5 centimeters join to form a single nerve which bifurcates at the base of the trigone (Fig. 3). The intermesenteric nerves may enter the interiliac trigone widely separated and continue downward in this relationship to the base of the trigone, where they continue as the inferior hypogastric nerves, thus giving a bilateral (or double) cord pattern (Fig. 4). When this occurs, the cords have a number of very fine filamentous connections demonstrable throughout the length of the interiliac trigone (8 per cent).

Plexus patterns occur (4 per cent) wherein the lateral components are sharply marked but there are numerous heavy connecting fibers, and though the nerve fibers when inadequately dissected appear as a single flat band, careful dissection reveals a plexus (Figs. 5 and 6).

In many instances (29 per cent) the intermesenteric nerves upon entering the trigone fuse and almost immediately bifurcate to diverge at an acute angle. The diverging nerve cords are connected by many fibers, and a narrow triangular pattern results (Fig. 7), in contrast to the more frequent (35 per cent) and similar though wider triangular pattern and the relatively rare (2 per cent) spider-web pattern (Fig. 8) which is found when the divergence is marked and the connecting fibers are numerous and fine. In only 2 dissections (1 per cent) were arch shaped patterns encountered (Fig. 9).

The plexus may be shifted so as to occupy a position solely to the left of the midline (Figs. 10 and 11). However, the infrequency (8 per cent) of the occurrence of this left-sided "shift" certainly makes unacceptable Reynolds' statement that "the nerves which comprise the so called hypogastric nerve pass caudally a little to the left of the midline." These "left-sided" plexuses were frequently found to be immediately adjacent to the left common iliac artery and the root of the sigmoid mesocolon. This is of considerable surgical interest since the extirpation of the retroperitoneal fibro-adipose tissue in the central portion of the interiliac trigone would fail to remove the nerve fibers constituting this type of plexus. An appreciation of the foregoing fact and that a single "presacral" nerve rarely exists; that the superior hypogastric plexus is always prelumbar and frequently occupies the entire interiliac trigone, will cause fewer failures to be reported after superior hypogastric plexus sympathectomy. The incomplete extirpation of the plexus, the improper selection of cases and to a lesser extent the occurrence of neuromas in the remaining nerve stumps being the chief causes of poor results in surgery of the superior hypogastric plexus.

In 8 per cent of the subjects the intermesenteric nerves continued into the trigone as multiple parallel bands, frequently fusing just before reaching the promontory of the sacrum to form the inferior hypogastric nerves. These multiple parallel cords or bands were connected by many fibers.

After a consideration of the large variety of patterns and the variations within each pattern group, one can well endorse the statement "It is difficult to find two plexuses with the same anatomical architecture" (Labate).

SURGICAL ANATOMY

A consideration of the surgical anatomy of the superior hypogastric plexus necessitates an appreciation of: (1) the interiliac trigone, in which the fibers of the plexus are always found; (2) the normal contents of the trigone; (3) "abnormal" contents of the trigone; and finally (4) the variations in the pelvic mesocolon.

The interiliac trigone has for its apex the bifurcation of the abdominal aorta, its lateral boundaries the common iliac arteries, and its base corresponds to a line joining the two common iliac arteries at the level of the promontory of the sacrum. The trigone, therefore, embraces an area comprising the lower half or third of the fourth lumbar vertebra, the intervening intervertebral cartilaginous disc and the fifth lumbar vertebra. Its length varies with the level of bifurcation of the abdominal aorta and averages approximately 6 centimeters (4.9 cm. to 6.4 cm.). It tends to be slightly more elongated in the male (by approxi-

mately 0.3 cm.). The width of the base of the trigone averages approximately 7 centimeters (5.8 to 7.5 cm.) and tends to be wider in the female than in the male (by approximately 0.5 cm.). This is in keeping with the normal divergence of the common iliac arteries from the bifurcation of the abdominal aorta, which occurs at an angle of 60 degrees in the male and 68 degrees in the female. It is of interest to note that the dimensions of the trigone were exactly similar in the negro and white female; however, in males the trigone tends to be narrower and longer in the negro than in the white.

The trigone normally contains the left common iliac vein, the middle sacral artery and veins, and the right ureter. On the left border of the trigone the inferior mesenteric artery and its sigmoid branch enter the root of the pelvic mesocolon. Finally a fairly tough retroperitoneal connective tissue layer, into which the fibers of the superior hypogastric plexus are incorporated, lies within this area.

The left common iliac vein runs parallel to the inferior (medial) margin of the left common iliac artery and courses upward and to the right, ascending posterior to the right common iliac artery to join the right common iliac vein in the formation of the vena cava. The left common iliac vein thus occupies a considerable portion of the upper and left aspect of the trigone. The vein is immediately subjacent to the overlying (anterior) layer of fibrous and fatty tissue in which the fibers of the superior hypogastric plexus are found and thus constitutes a surgical hazard of marked importance, especially when it is remembered that the wall of the vein is extremely thin. Fortunately, the fibrocellular layer which is firmly adherent in the remainder of the trigone is very loosely adherent to the vein and may be easily separated from it. An appreciation of the surgical importance of this fact is heightened when it is recalled that in 9 per cent of this series the entire superior hypogastric plexus is shifted to the left and occupies an area solely in the left half of the trigone being markedly condensed anterior to the left common iliac vein. In performing a superior hypogastric sympathectomy the surgeon working "over" (i.e., anterior to) the vein takes advantage of this loose connection of the nerves to the vein, in an effort to avoid injury to the vessel. Injury to the vein has been reported (1).

The middle sacral artery and its accompanying veins descend from the bifurcation of the aorta to the tip of the coccyx. The artery passes downward in the interiliac trigone which it tends to bisect, though occasionally it occupies a position slightly in the left half of the trigone. Within the trigone it lies successively upon the intervertebral disc between the fourth and fifth lumbar vertebrae, and the anterior aspect of the body of the fifth lumbar vertebra. It is posterior to the connective tissue layer which contains the nerve fibers, and may be palpated through this layer. The artery is not infrequently confused with a "single presacral nerve" type of superior hypogastric plexus and occasionally has been extirpated for the plexus. It is interesting to note that the *artery* which is *not frequently visually obvious* can almost invariably be palpated, while the *nerve fibers* of the superior hypogastric plexus which *are frequently visually obvious* through a transparent peritoneum can not be identified by the palpating finger. When this point is appreciated more fully, the incidence of extirpation of the middle sacral artery for the "presacral nerve" will markedly decrease. An appreciation of the fact that the existence of a "presacral nerve" is in itself a rarity will also cause a cessation of the extirpation of a single cord area, and lead to the universal adoption of the policy of extirpating the entire interiliac fibrocellular tissue for removal of the superior hypogastric sympathetic plexus.

The right ureter is exposed in the interiliac trigone, where it crosses the right common iliac artery just superior to its bifurcation into the external iliac and hypogastric arteries. Fortunately, the right ureter is firmly adherent to the posterior surface of the peritoneum and is usually retracted with the peritoneum when it is reflected laterally, whereas the nerve fibers are incorporated into and firmly adherent to the subjacent fibrocellular layer of retroperitoneal connective tissue. Thus the ureter can be identified and injury to it avoided. In certain instances in which a type III mesocolon exists (*vide infra*) and it is necessary to retract the mesocolon sharply to the left, or when a type II pelvic mesocolon exists which must be retracted far to the left in order to remove it from the operative field, the ureter may be displaced mesially and be more liable to injury. The left ureter is normally found entirely outside of the interiliac trigone and is rarely subject to injury in superior hypogastric sympathectomy.

The inferior mesenteric artery runs downward from its origin about 3.5 centimeters superior to the bifurcation of the aorta, running obliquely and to the left, anterior to the lower portion of the abdominal aorta, and the left common iliac artery. It descends into the pelvis between the layers of the sigmoid mesocolon to terminate on the rectum as the superior hemorrhoidal artery. Its sigmoid branches run downward and to the left to enter

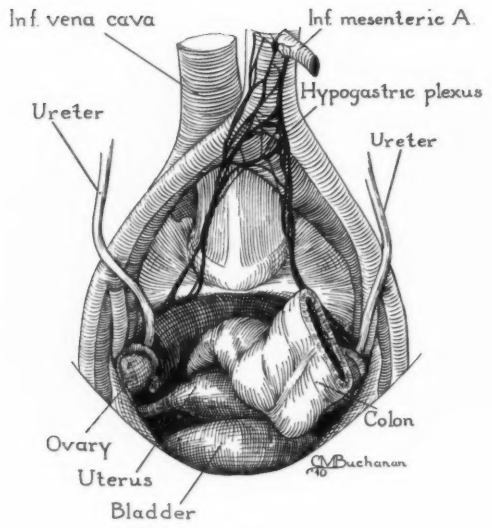

Fig. 12.

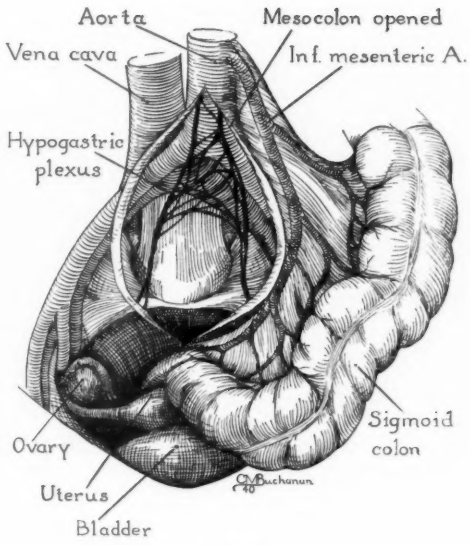

Fig. 13.

the sigmoid mesocolon and are distributed to the sigmoid. As they enter the root of the pelvic mesocolon they lie on the left border of the interiliac trigone and in instances in which a type III mesocolon exists they assume importance in superior hypogastric sympathectomy since it is necessary to dissect between the layers of the mesocolon to expose the interiliac trigone, and in such a dissection these vessels may be injured.

The interiliac trigone is entirely retroperitoneal. Its peritoneal covering on the right is reflected to the lateral walls of the pelvis and spreads downward to the anterior surface of the sacrum. On the left the peritoneum descends from the abdomen to the rim of the pelvis where it is reflected over the sigmoid colon and the upper portion of the rectum whence it is again reflected to the inner aspect of the anterior abdominal wall. The peritoneal layers which have thus ensheathed the pelvic colon approach each other superomedially and fuse to form a true mesentery, the pelvic mesocolon. Between the two layers of the pelvic mesocolon run the vascular and nervous supply of that section of the bowel.

There is considerable variation in the length and the position of the line of attachment of the pelvic mesocolon. In general three main types may be described:

Type I. A short mesocolon easily retracted to the left and allowing adequate exposure of the interiliac trigone (Fig. 13).

Type II. A long mesocolon which may readily be shifted or retracted to expose the interiliac trigone (Fig. 14).

Type III. A long mesocolon, the leaves of which embrace the interiliac trigone; its attachment being along the midline. This type of mesocolon makes difficult the exposure of the interiliac trigone, particularly when dissection between the leaves of the mesocolon is resorted to in order to expose the superior hypogastric plexus (Fig. 15). This type of dissection endangers the vascular and nervous supply which is transmitted through the mesocolon to the bowel it ensheaths. Dissection between the layers of the mesocolon should be avoided and the superior hypogastric plexus exposed by incision parallel to the root of the mesocolon and through both of its layers (Elaut). In a series of 50 dissections Elaut reported the occurrence of 78 per cent of the first type of mesocolon, 14 per cent of the second, and 8 per cent of the third. Roussel reported type III mesocolon in 15 per cent of his cases, while Cotte found it in only 1 per cent. Bernard and Theodoresco, and Labate have each reported its occurrence in 1 case.

In this series in females type I occurred in 75 per cent, type II in 25 per cent. Type III did not occur. The incidence was similar in the negro and the white. However, in males there was a greater occurrence of the type III mesocolon in the negro, the percentages being 82 of type I, 14 type II, and

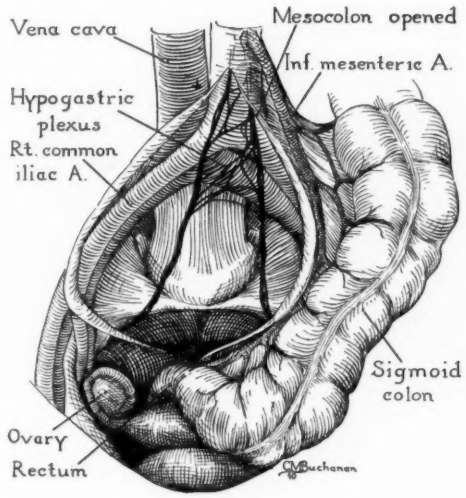

Fig. 14.

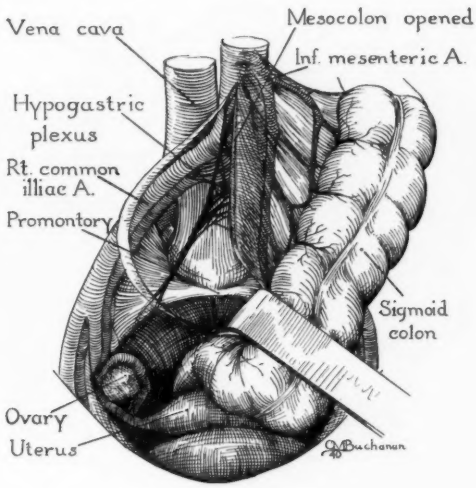

Fig. 15.

5 type III in the white, while they were 70 type I, 16 type II, and 14 type III in the negro. As previously noted this was the only significant racial difference encountered.

In addition to these normal relations of the interiliac trigone, various anomalies have been encountered. In 4 dissections accessory ureters were found which traversed the trigone. Davis similarly reported occurrences of accessory ureters in 3 of the 12 operative cases he studied. In several of our dissections in the infant, the right ureter bent rather sharply toward the midline and so was included in the trigone and subject to injury. This finding is confirmed by Labate, who included 52 infants in his report of 75 dissections.

In 3 of our dissections the transverse duodenum was found anterior to the interiliac trigone. In 1 of these cases the other abdominal viscera were also ptosed. In the 2 others the abdominal viscera were normally located with the exception of the duodenum. The left common iliac vein in 14 per cent of our dissections had sharp S-like deviations toward the midline, and projected into the interiliac trigone to well beyond the midline occupying the entire upper and left half of the trigone. In 2 per cent of this series the left common iliac artery had a similar deviation, and occupied a position which would normally be well within the interiliac area. In these 2 instances the artery was partially covered anteriorly with the hypogastric plexus which in each of these instances was of the spider-web pattern, and occupied an area comparable to the normal trigonal area. In 1 subject the right and left common iliac veins joined to form the inferior vena cava anterior to the bifurcation of the abdominal aorta. The interiliac trigone in this instance was bounded by the vena cava superiorly and the common iliac veins laterally, the aorta and common iliac arteries being posterior to these structures. The superior hypogastric plexus in this instance was of the multiple cord pattern and within the venous triangle.

The discussion of a very important vascular anomaly which occurs with surprising frequency and which has gained little attention in the literature has been left for last. The majority of investigators are silent on the subject. Elaut states "One must bear in mind a certain anomaly of the blood vessels occurring not infrequently within the interiliac trigone. In our rather small series of cases we met this condition twice, namely: a large, pencil-sized vein arose from the left common iliac vein, proceeded directly across the trigone and joined the opposite wall of the pelvis at a spot close to the bifurcation of the common artery. The veins lay on the periosteum, the nerves cross it obliquely, being adherent in a few places." In the series of dissections herein reported anomalous veins of this type were found 26 times! Seventeen occurred in the male, and 9 in the female, with the distribution even between the negro and white. In several instances the vein was half as large as the common iliac vein, while in the greater number of cases the vein was of much smaller size. In 3 instances these large veins arose within the substance of the psoas

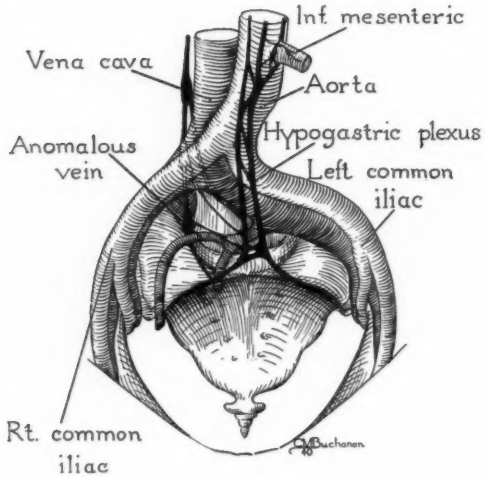

Fig. 16.

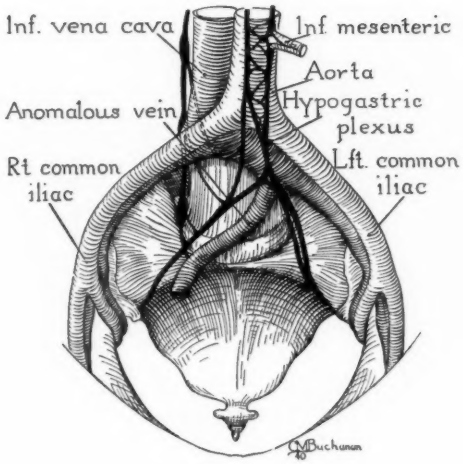

Fig. 17.

muscle on the opposite side of the pelvis and crossed the interiliac trigone to empty into the left common iliac vein. Many of the smaller veins could be traced directly from the periosteum traversing the interiliac trigone and emptying into the common iliac vein. Several of the veins were in the nature of accessory hemorrhoidal veins which ran retroperitoneally to the left of the midline in the interiliac trigone to empty into the left common iliac vein. These veins are a distinct surgical hazard, and should be given much greater emphasis. Further investigations of their exact origins are in progress (Figs. 16, 17).

RESULTS OF EXTIRPATION OF THE SUPERIOR HYPOGASTRIC PLEXUS

A detailed account of the physiology of the superior hypogastric plexus does not come within the province of this paper. However, one hesitates to omit some comments on the results of extirpation of the superior hypogastric plexus on menstruation and on parturition which are currently not widely appreciated. Despite many expressed fears to the contrary, Pearce has recently adequately stressed the lack of harm of this procedure in reference to childbirth and concluded, "Presacral neurectomy has no influence on any part of the process of pregnancy. In some patients, probably only a small proportion, the first stage of labor is painless and rapid or else unobserved." These conclusions are substantiated by the observations of many others (Collins, Cotte, Davis, Donaldson, Keene, Learmonth, Fontaine and Herrmann, and Wetherell).

The menstrual cycle is unaffected by superior hypogastric plexus sympathectomy, though the period immediately following the operation may be prolonged (Fontaine and Herrmann).

The physiology of the superior hypogastric plexus in relation to the urinary system has been adequately stressed by McLellan and Learmonth.

SUMMARY

A report is given of 150 personal dissections of the superior hypogastric plexus: 20 females, 14 negro and 6 white; and 130 males, 96 negro and 34 white. The surgical anatomy of the interiliac trigone, an area bounded by the bifurcation of the abdominal aorta, the common iliac arteries, and the promontory of the sacrum, which contains the superior hypogastric plexus, is described. Stress is laid upon:

1. The wide variation in the configuration of the superior hypogastric plexus and the predominance of plexus patterns, 88 per cent; the uncommon finding of bilateral nerve cords, 8 per cent; and the relative rarity of the single "presacral nerve," 4 per cent.

2. The disposition of the normal contents of the interiliac trigone; (a) the left common iliac vein; (b) the middle sacral vessels: (c) the right ureter; and (d) the fibrocellular connective tissue lamina which contains the superior hypogastric plexus (Fig. 12).

3. The anomalies of the interiliac region: (a) accessory ureters; (b) low lying transverse duodenum covering the anterior surface of the trigone; and (c) an anomalous vein which occurred in 26

dissections to which special emphasis is given (Figs. 16 and 17).

4. The variations in length and implantation of the sigmoid mesocolon with a description of the three types encountered (Figs. 13, 14, and 15).

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SO CALLED "IODINE RESISTANT" HYPERTHYROIDISM

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THE operative mortality rate in well controlled cases of hyperthyroidism is still between 1 and 5 per cent depending upon the co-ordination between the medical and surgical divisions and the number of severely ill patients included in the series studied. We do not consider the patient with Graves' disease an emergency until he has been started on iodine; even the acutely ill patient can be controlled for a period of time with diligent medical and roentgen therapy. A few cases of toxic goiter, between 5 and 10 per cent, will not respond to the usual preoperative iodine therapy and some appear to become definitely worse with its use. These patients are usually in the older age group and it is our opinion as well as that of others, that the mortality and morbidity following operation in these cases are higher.

We wish to show that these so called "iodine-resistant" or "iodine fast" cases will respond to a specific regimen of therapy, that they are not emergency cases, but that with time they can be operated upon under the influence of iodine. Blank, Means, and others have definitely found, both by clinical and pathological studies, that some of these patients are in reality being controlled by iodine. There is no clinical evidence of this fact, however, because the use of the iodine is preventing a crisis. Crisis, in itself, would suggest that great caution should be exercised in anticipating operation at this time.

A search of the literature reveals that this condition was not described until after Marine and Kimball in 1917 advocated the use of iodine and iodized salt in the prevention of "endemic" goiter, and when Plummer and his associates recommended in 1923 the use of Lugol's solution in the preoperative and postoperative care of toxic patients. It is obvious to us that some of these patients have been taking sufficient iodine so long that the thyroid is no longer able to respond to its use. The source of the iodine may be salt, food, old family remedies, or patent medicine. W. O. Thompson et al. have shown that the minimal effective dose of compound solution of iodine varies between 6 and 10 milligrams a day. The average person consumes about 1.2 milligrams of iodine a day in table salt alone without considering other food sources. It is a well known fact that if a patient has been receiving Lugol's solution or some other iodine substance for a long time in an attempt to manage his condition "med-

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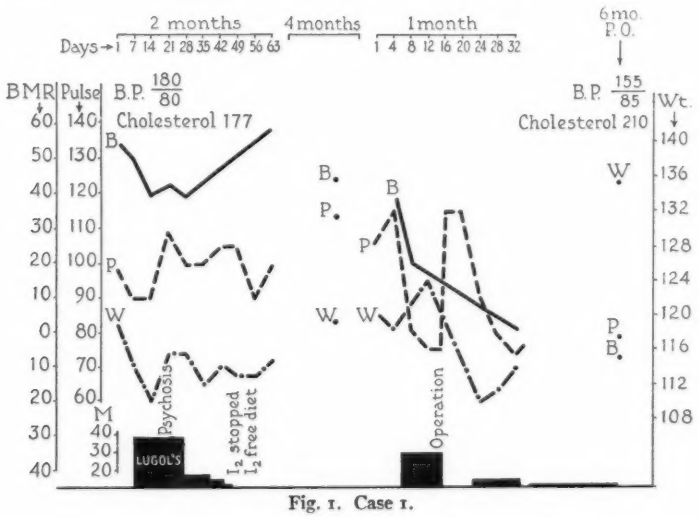

Fig. 1. Case 1.

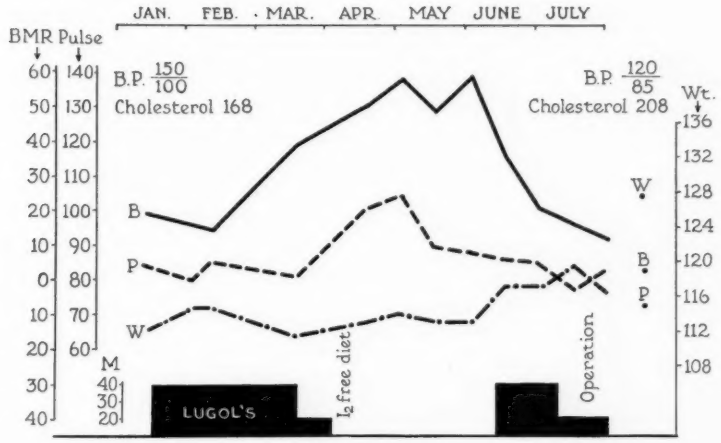

Fig. 2. Case 2.

ically," the only *safe* way to treat that patient further is to take him off iodine *gradually*. Then after a period of time, say 2 to 4 months, when the thyroid will again respond the patient can be operated upon safely under its influence.

With this in mind, we suggest the following regimen to be used in such cases. When it is obvious that a patient will not have an "iodine remission" he is weaned from it, so to speak, that is, the iodine is stopped gradually so that a crisis will not occur. The weaning process may take a few days or it may take weeks. The symptoms may become slightly aggravated but bed rest and sedation have been found ample to control them. The x-ray may also be helpful. Second, the patient is placed on an iodine-free, or low in iodine, diet but high in proteins, vitamins, and carbohydrates. It must be emphasized again and again to the patient not to take iodine or any foods containing it and to take no medicine other than that prescribed. The patient may be seen at weekly intervals for the first month or so and then every month until sufficient time has passed, 2 to 4 months. At the end of this time he is again hospitalized and prepared in the usual manner for operation.

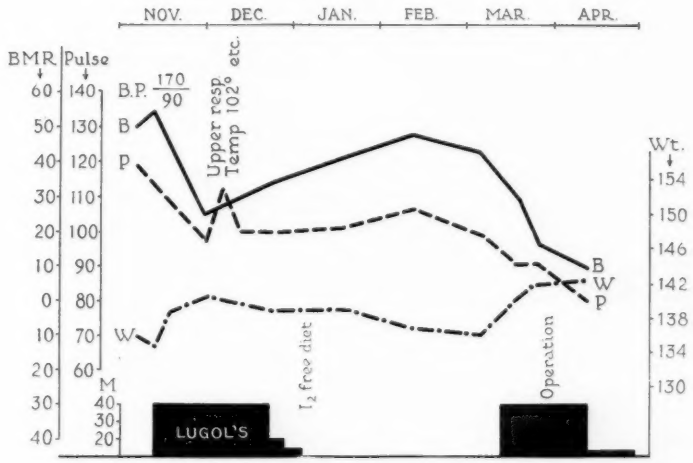

Fig. 3. Case 3.

Brief reviews of 2 cases with their clinical records are presented to show the efficacy of this method. A third case is presented to demonstrate the value of the method in a patient who developed a preoperative complication that made postponement of surgery to a more opportune time necessary.

CASE 1. Mrs. H. H., 50 years of age, sought relief for palpitation, loss of weight, nervousness (hysteria at times), heat intolerance, and eye trouble. There was no history of iodine medication for 12 years. Physical examination showed a nervous, acutely ill female; pulse, 100; blood pressure, 180/80. The skin was hot and moist with a definite pigmentation over the forearms. She presented a moderate exophthalmos and had numerous eye signs. A firm thyroid was palpable, but there was no bruit. Laboratory reports were essentially normal except for a metabolic rate of plus 54 per cent. From a study of the chart (Fig. 1) it can be seen that on Mrs. H's first admission to the hospital there was little, if any, response to 28 days on iodine therapy so this was stopped gradually and the patient was discharged from the hospital. Four months later she was readmitted to the hospital and was operated upon successfully following an iodine remission. It is interesting to note the postoperative reaction following the abrupt withdrawal of iodine and its subsidence when iodine was started again.

CASE 2. Mrs. A. G., 46 years of age, also had a rather typical history and findings of toxic goiter, with no previous story of iodine medication. The physical findings showed a nervous, well developed, white female; pulse, 95; blood pressure, 158/70. The thyroid was enlarged, with a slight bruit, firm, and nodular. In this patient's clinical course (Fig. 2) she was one of the few that we have seen who developed more severe toxic symptoms while on iodine, but after a period of 3½ months without it we were able to secure a remission and she was safely operated upon.

CASE 3. Mrs. J. F., aged 50 years (Fig. 3), presented clinical symptoms and findings of Graves' disease. She developed an acute upper respiratory infection on the fifteenth day of preoperative preparation, and had escaped from the iodine effect by the time this was controlled. The patient was sent home on an iodine-free diet, etc., for 3 months and has since been readmitted to the hospital and successfully operated upon.

CONCLUSION

The 3 cases presented show the benefit of the conservative handling of so called iodine-resistant cases as well as in one in which postponement of operation was necessary.

We realize the difficulty of managing these patients unless they can be kept under constant observation but do believe that in cases not emergencies, the type of care described will result in a further reduction in mortality and morbidity.

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HAZARDS OF FIRE AND EXPLOSION OF ANESTHETIC AGENTS

II. In the Presence of the Cautery

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WE have described, in a preceding report,[1] the hazard of anesthetic combustion during the use of x-ray apparatus. Like x-ray equipment, the cautery is a common source of danger that is always condemned by writers on anesthetic explosions but without sufficient explanatory detail to force every anesthetist and surgeon to realize how serious is the danger and how great is the need for accurate and minute knowledge of the facts of anesthetic combustions. In this paper we deal at length with the information required of the anesthetist and the surgeon which will enable them to use the actual cautery safely and yet without unnecessary restrictions.

We also discuss here, because it is most fitting, ignition by such obviously hot objects as the cautery, gas flame, match light, or cigarette; also mentioned are the small group of fires caused by the application of the cautery to surgical fields prepared with ethyl chloride spray anesthesia, or with inflammable skin cleansers like ether or alcohol, or with inflammable skin antiseptics like the various tinctures.

The actual cautery is an important surgical instrument employed in almost every operating room at least several times a week. Familiarity with the cautery has bred contempt for this hazard. On the other hand, unreasonable restrictions against the use of the cautery should not be placed in the way of the surgeon desiring to employ it.

Why have there been at least 55 known and wholly preventable anesthetic fires and explosions ignited by such an obvious hazard as a cautery, flame, or other hot object? We think the explanation is to be sought in the following reasons:

1. Ignorance of an elementary knowledge of anesthetic combustion. Our personal survey has found an astonishingly large number of surgeons and anesthetists who lack basic and even rudimentary information on this subject.

2. Indifference toward the hazard because of past good fortune while using set-ups in the operating room which we consider dangerous.

3. A paucity and inflexibility of anesthetic methods available to many surgeons who must use the cautery. (*This is the usual reason for the use of hazardous techniques.*)

In short, the cause is almost always ignorance. The cure must be education and elevation of the standards of anesthetic training and practice.

PHYSICAL AND CHEMICAL DATA

The fundamental physical and chemical data included in the first report (22) will not be repeated, although they should be familiar to all who read this and subsequent reports. We shall, however, present such supplementary facts as have a special bearing on the particular type of hazard under discussion.

The following information, added to the basic scientific facts presented in our first paper, should be required knowledge of every anesthetist, and also of every surgeon who desires or is obliged to dictate the choice of anesthetic procedures.

1. The minimum ignition temperatures at 0 degrees C. are shown in Table I.

TABLE I.—MINIMUM IGNITION TEMPERATURES

	In air	In oxygen
Diethyl ether	304	182
Divinyl ether	399	327
Ethylene	490	485
Cyclopropane	498	
Ethyl chloride	517	468

It is apparent that the presence of a high concentration of oxygen instead of air (21 per cent oxygen and 79 per cent nitrogen) lowers the minimum ignition temperature of a combustible agent; nitrous oxide lowers it even more than does oxygen (8).

As shown in Table I ether-oxygen and ether-air mixtures are more easily ignited than similar mixtures of ethylene or cyclopropane.

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[1]This is the second of a series of papers on the explosion and fire hazard of anesthesia based on a study of the literature and of the case reports secured by the Committee on Anesthetic Hazards, Dr. Barnett A. Greene, chairman; this group acting as a subcommittee of the Research Committee of The American Society of Anesthetists, Inc.

The minimum ignition temperatures of liquid ether, and mixtures of ether with air, oxygen or nitrous oxide are well below visible spark temperatures (3, 4, 13). Kirby Thomas has found that certain mixtures of ether-air or ether-oxygen can be exploded at temperatures below 100 degrees C. (33).

The hot element of all cauteries can ignite any combustible anesthetic mixture. Many case reports have demonstrated this fact beyond doubt.

2. Electric cauteries present four points at which igniting temperatures may be produced: (a) the heated element, (b) the foot pedal switch, (c) the rheostat, and (d) the cord or terminals which may break because of frequent usage or become detached because of inadvertent pulling (29), thus producing sparking.

3. A knowledge of the densities of anesthetic gases and vapors is important in understanding the cautery hazard. As compared with air having a density of 1, ethylene has a density of 0.97; cyclopropane, 1.45; ethyl chloride, 2.23; divinyl ether, 2.42; and diethyl ether, 2.56 (21).

"The rate at which a gas or vapor will diffuse or mix with air is inversely proportional to the square root of its density (rate of diffusion $\propto \frac{1}{\sqrt{\text{Density}}}$); for this reason anesthetics having low density such as ethylene will diffuse more rapidly into air than will ether vapor. This means that rich mixtures of ethylene on being discharged into an operating room will pass through the explosion range and become nonexplosive, other conditions being constant, sooner than a heavy vapor. . . . A heavy vapor such as ether has a tendency to remain longer in its highly concentrated condition and on account of its greater density will tend to descend and accumulate at the floor level and under favorable circumstances may flow a considerable distance from the source of discharge. On account of these characteristics, the fire hazards are greater for vapors of this type. . . ." (21). Ether has been known to take fire at a measured distance of 15 feet from the source of escaping vapor (34).

It is because of its heavy density as well as its frequent administration in open techniques that we find ether to be the most often ignited anesthetic when the igniting agent is external to the anesthetic circuit, e.g., cautery, faulty electrical apparatus, and flames.

The actual concentrations of ethylene in the atmosphere of operating rooms has been well studied by Cheney and Folkman. Based on several thousand readings made in 4 hospitals of modern construction but without unusual ventilating systems, the conclusions of their report are worth repeating here (4).

"a. At distances of 10 feet or more from the patient's head the concentrations were so small as to be indeterminable.

"b. No evidence of accumulation of ethylene percentages in any part of the operating room was found after the longest period of continuous anesthesia (with the partial rebreathing method of administration).

"c. Electric switches on the walls of the operating room were shown to be entirely harmless inasmuch as the maximum ethylene concentration at these points was less than 0.1 per cent.

"d. The only points where explosive concentrations of ethylene occurred were in the immediate vicinity of the face mask. The 'dangerous area' extended to 1 foot above the face mask and 2 feet to the particular side of the mask toward which the expiratory vent pointed. Immediately to the side of the mask but on the side opposite that toward which the vent was directed the ethylene concentration was less than 1 per cent.

"e. With the vent of the exhalation valve pointed to the side, no concentration above the chest of the patient was found higher than 0.2 per cent in those cases in which the anesthetist used a cloth shield between the field of operation and the patient's head. These percentages were also reduced when the anesthetist used rebreathing.

"f. With the use of a cloth shield, proper adjustment of the exhaling vent and the technique employed by the anesthetist during these tests, it would appear that the cautery could be used in the abdomen with entire safety." (The technique used in these tests included a tightly fitting mask, exhalation vent directed to the side and not straight up, and, most important, a large percentage of rebreathing.)

Since the time of these studies (1930) the method of complete rebreathing has become standard practice. With this method the atmosphere of the operating room is more likely to be free of an explosive concentration of ethylene or any other anesthetic, even in the region close to the mask. But sudden, unexpected breaks in the closed circuit because of vomiting, the need to use suction or to insert an airway, preclude the possible use of the cautery or a flame near the head, neck, shoulders and chest, even with a perfectly closed circuit (a theoretical assumption that is frequently not attained in clinical practice).

4. Exact information on the combustibility of the expirations of a patient under anesthesia and the duration of its inflammable status is needed to enable the anesthetist to know when the surgeon

may safely apply the cautery in the region of the head after an inflammable anesthetic mixture has been administered. This situation, expected or unexpected, is frequently encountered. Many case reports testify to the incorrect answer to the question and record the consequent death of the patient.

The duration of the period in which an etherized patient exhales an inflammable concentration after the administration of ether has ceased depends on the minute-volume of respirations and the degree of saturation of the patient with ether. The expired breath of a patient in third stage anesthesia *immediately* after the end of administration of ether-air, ether-oxygen or ether-nitrous oxide-oxygen is probably combustible. This may be inferred from the data of anesthetic concentrations compared with the figures for explosive concentrations; for the concentration of ether for the induction and maintenance of anesthesia is at least 2.5 per cent, more often 3.5–4.5 per cent (1); and the lower limit of inflammability of ether in air is 1.85 and of ether in oxygen is 2.10 (21). Furthermore, as long as the patient remains in full surgical anesthesia we might expect to find an inflammable percentage of ether in the breath. This deduction is based on the data quoted by Beecher from the research work on dogs by Haggard and Robbins (1). They have shown that surgical ether anesthesia is induced and maintained with 3.7–4.5 per cent ether in the respired air; that this produces a blood ether concentration of 100–120 milligrams per 100 cubic centimeters of blood; and that light (first plane) surgical anesthesia corresponds with an arterial blood ether content of 115 milligrams per 100 cubic centimeters (1).

These inferences are contradicted (a) by the statement of Hewer that "the exhalations of an etherized patient are probably never inflammable or explosive" (19); and by (b) the report of Hasler (17) that samples of air taken at a distance of 2 inches from an open mask, after an operation had been in progress for an hour and 10 ounces of ether had been used, were noncombustible; and (c) by the work of Featherstone and Morgan (9, 27) who were unable to ignite, by spark or flame (1) specimens of expired air and ether collected immediately after the withdrawal of a heavily impregnated ether mask, (2) collected expirations during deep ether anesthesia, or (3) a mixture exhaled immediately after a deep inspiration of a strong ether-air mixture.

Despite these negative and reassuring reports, we must take a skeptical attitude because in addition to the danger theoretically inferred from explosive and anesthetic concentrations, we possess case reports which testify to the reality of the danger. Even Featherstone is not sure of the safety of his findings as indicated by his advice that the patient under ether should be allowed to take a dozen breaths of fresh air after the administration of ether has ceased (9). We feel, however, that such a practice is too unreliable (because the rate of exhalation of ether may be very variable) on which to depend for an act so hazardous as applying a cautery in or near the head of a patient who has had ether.

To resolve the inevitable doubt at a time when it is urgent and important to know positively whether or not the expirations of a patient are inflammable, we recommend the simple method suggested by Flagg (10). He has advised the withdrawal of a sample of the expired pharyngeal air by means of a bulb syringe and the testing of the inflammability of its contents in an adjoining room by emptying the syringe across an alcohol lamp flame. An inflammable mixture changes the color of the flame by taking fire; an explosive mixture harmlessly "pops." In place of the 2 inch rubber bulb fitted with the glass top of an eye dropper which Flagg has used, we prefer, as safer and simpler, an all-rubber ear syringe of the same size. There is no possibility then of shattering glass or of the glass tip slipping out of the bulb handle. This test is simple, safe, and positive in its results. If the test, which we shall hereafter refer to as the Flagg test, is negative then "the field is absolutely safe for cauterization at that time" (10).

An important fact, related to the safety of using a cautery near the head of an etherized patient, is that the stomach may contain an inflammable concentration of the anesthetic swallowed during induction. This is much more likely with ethylene and cyclopropane than with ether (which is administered in concentrations not much above the minimal limit). The stomach bubble of combustible gases may be regurgitated during the period when the patient is breathing fresh air and is ascending from surgical anesthesia. At this critical moment the cautery might be applied in or near the head of the patient. Thus there might occur an explosion under conditions considered safe because the patient had been allowed to take a dozen breaths of fresh air and the Flagg test had been found negative only a few seconds or a minute before. Therefore, if an igniting agent such as a cautery or hot metal dental syringe must be used in the upper respiratory tract after the patient has received a combustible anesthetic, it is necessary to deflate the stomach by intubation before securing a negative Flagg test.

The respiratory tract a of patient in third stage anesthesia under ethylene-oxygen probably does not contain an explosive mixture because the concentration of ethylene is in the range of 85 to 90 per cent whereas the upper limit of explosive concentrations of ethylene in oxygen is 79.9 per cent (21). Within a few breaths of air or oxygen, however, the explosive range is reached. The exhalations of a patient under cyclopropane oxygen are always inflammable, just as is true of ether, because the anesthesia concentrations are always in the inflammable range. As to how long the respiratory tract contains an inflammable mixture after the cessation of administration of ethylene or cyclopropane, there are no definite data; but one should apply all the precautions advised here for ether; namely, the breathing of fresh air, the use of the Flagg test, and intubation of the stomach.

The preceding discussion of facts, which might be of value when the cautery is to be used in or near the head of a patient who has received a combustible anesthetic, should not be interpreted to mean that we believe this to be good practice. When any igniting agent is to be employed in such a dangerous location, it is far safer, and it is our invariable rule, to use a noncombustible anesthetic technique. But there have been and will be many instances when, after an inflammable anesthetic has been given, the surgeon is suddenly and unexpectedly required to use a cautery, fulguration, coagulation, etc. In such circumstances, the information which is given here will prove to be invaluable.

CLINICAL DATA

Most writers flatly object to any use of the cautery in the presence of combustible anesthetics. Others have employed the cautery with only few precautions. For example, Horsley (20) has reported using the cautery in 41 of his first 116 anesthesias with ethylene-oxygen with only partial rebreathing without any trouble "although care is always taken to increase the operating room ventilation temporarily while the cautery is being used and the cautery is never used near the mask nor in operations on the head or neck." Yandell Henderson (18) has stated "the use of the cautery in the abdomen (with ethylene and partial rebreathing) is safe only when a screen or curtain is placed between it and the patient's face." Personal communications from many surgeons of long experience have described the long and uneventful use of ether by open drop or partial rebreathing administration during cauterization in the abdomen, pelvis, and perineum. It is to be expected that those who practice or allow the practice of anesthesia with carelessness, or who are ignorant of its hazards are not likely to submit reports to the literature or scientific societies; and therefore, just those in greatest need of criticism and correction avoid them.

On one point all authorities are agreed: "Under no circumstances can any cautery or other spark producing equipment be used around the head of the patient or the pleural cavity, when the patient has been anesthetized with any inflammable anesthetic. To do so is criminal negligence" (29). Despite this unanimity of opinion, we have been able to find in at least 26 of the 55 cases of combustion reported in this paper due to the cautery and flame that the igniting agent was used under conditions which would be considered today to be "criminally negligent."

Many authorities realize that it is not practicable to prohibit any and all use of the cautery in the presence of a combustible anesthetic (27, 30). A large number of leading anesthetists have admitted using cyclopropane, ethylene, or ether by closed circuit administration during the application of a cautery in abdominal operative procedures (5).

It is imperative that we formulate what we consider a safe and practicable set of principles governing the use of the cautery in the operating room. After a study of the physical and chemical data, the published and unpublished reports of others and as a result of his own experiences, observations, and discussions with leading anesthetists, the writer has formed the following opinion:

1. The anesthetist should specifically inquire before the start of the anesthesia as to the possible use of the cautery.

2. If the cautery must be used on or in the head, neck, shoulder, chest, respiratory passages or pleural cavity, the anesthetic must be of a noncombustible type (e.g., regional block, nitrous oxide, intravenous barbiturate or rectal basal anesthesia or combinations of two or more of these). The use of chloroform is to be avoided because it is decomposed by heat to form irritating fumes (30).

3. If the cautery must be used in the abdomen, pelvis, perineum, lumbar back, lower extremities or distal parts of the upper extremities, the anesthetic of choice should be of a noncombustible type, provided it is as safe, from all other viewpoints, for the patient as would be the combustible inhalation anesthetic that would have been chosen had the surgeon not used the cautery.

4. If the cautery must be used in those regions listed in paragraph 3 and a combustible anesthetic must be administered (because of the condition of

the patient, the type of surgery, or the limited experience and ability of the available anesthetist), then the following conditions should exist before the cautery is switched on:

a. *A meticulously closed circuit* method of administration should have been in use during the prior 10 minutes, an arbitrary but clinically determined safe period (13).

b. The combustible anesthetic of choice, if combustible it must be, is ether-air by closed circuit administration because of its smaller tendency toward propagation and smaller range of explosibility as compared with ether, ethylene, or cyclopropane mixtures with high concentrations of oxygen or nitrous oxide. Cyclopropane, ethylene and ether with oxygen are permissible, however.

c. The ventilation should have been arranged to increase the dispersion of anesthetic gases and vapors previously allowed into the atmosphere. The direction of ventilation should be away from the cautery and toward the patient's head.

d. The patient should be securely set in third stage anesthesia (deep first plane or deeper) to be certain that no vomiting occurs to break the closed circuit during the period of cauterization.

e. No part of the cautery, its wires, switch, or rheostat should be near the anesthetic apparatus.

f. A draped screen should be placed so that it will intervene between the head of the patient and the field of operation.

g. If doubt exists as to the freedom of the room from inflammable concentrations of anesthetics released into the air before the circuit of anesthetic administration is closed, then a "Flagg test" should be applied to the possible points of contact of the cautery apparatus with atmosphere.

5. If the cautery is to be used on or in a hollow viscus in the abdomen, such as the bladder or stomach, in addition to the precautions listed in paragraph 4, we advise, when ethylene, cyclopropane or acetylene is used, that one take pains to empty the viscus of its gaseous content just before the cautery is applied (13).

6. If the cautery is unexpectedly required in a case which has been inhaling a combustible anesthetic, the necessary precautions before the cautery is permitted are:

a. If the field of operation is on or in the head, neck, chest, or respiratory tract, the anesthetic should be changed to another but noncombustible type while the respiratory tract is ventilated with air and the stomach is emptied until the Flagg test is negative both at the field of operation and the atmosphere adjoining the cautery apparatus at any of its parts.

TABLE II.—SUMMARY OF 55 CASES

Agent	Total no. of cases	Cautery or flame used near head, neck, chest, etc.			Cautery or flame used in abdomen or elsewhere		
		No. of cases*	Deaths‡	Injuries‡	No. of cases*	Deaths‡	Injuries‡
Ether-air	12	3	1	2	2	0	0
Ether-O_2 (with or without nitrous oxide	17	7	4	5	5	0	2
Ether-air or O_2	6§						
Ethylene	9	6	5	4	2	0	3
Ether or ethylene or both	1	1	1				
Ethyl chloride	3				3	0	2
Acetylene	3				2	0	2
Cyclopropane	2§						
Alcohol	2	1	0	1	1	0	1

*The cases counted in this group are only those in which the presence or absence of injury is known.
‡The total number of persons injured or killed is stated; in some instances more than one person was injured. In no case was more than one person killed.
§One patient died—classification not possible for want of details of explosion.

b. If the field of operation is on or in the abdomen, pelvis, perineum, lumbar back, and extremities, the anesthetic may be continued with a closed circuit administration together with the precautions advised in paragraph 4 or the anesthetic may be changed to a noncombustible type with the precautions which are advised in paragraph 6a.

In the event of the situations described in either paragraphs 6a or 6b, proper ventilation away from the cautery and toward the head of the patient should be arranged.

We realize that these rules of conduct appear complicated; but they really are not any more than a detailed description and summation of modern anesthetic procedure as practiced by many leading anesthesiologists, and required of all who wish to avoid any of the accidents known to have occurred.

This description is an elaboration of the knowledge which Guedel assumes when he states the factors determining the use of the cautery in the presence of an inflammable agent as "appreciation of the weight of the vapor, the distance of this from the cautery, the amount of vapor freed into the room and the direction of air currents." The only unusual precaution we have added is the Flagg test which should be more widely and frequently employed to substitute proof of safety for guesswork. Of course, *the simplest and ideal*

precaution against explosions is to avoid all combustible anesthetics when the cautery or flame must be used in the operating room. The more experienced and versatile the anesthetist the more often is the ideal precaution practiced. But we must remember that many circumstances associated with the surgeon, patient, or anesthetist prevent the use of a noncombustible anesthetic everywhere and every time a cautery is employed.

CASE REPORTS

We possess the records of 55 cases of anesthetic[1] ignition by a cautery, flame, or similar hot object (Table II). These include all that were obtained by circularizing the members of the American Society of Anesthetists and by intensive searching of the literature. They are only a small fraction of the total number of such accidents of which the very great majority have remained untold for fear of criticism or litigation.

SUMMARY AND CONCLUSIONS

1. In this paper, the second of a series of reports on anesthetic combustion hazards, we have presented the physical, chemical and clinical data required for an adequate understanding of the dangers and the safeguards associated with the presence of a cautery or flame in the operating room.

2. Fifty-five anesthetic (and related) fires and explosions ignited by a cautery or flame have been collected. These are all the cases we could find after a survey of the literature and extensive questioning of members of The American Society of Anesthetists, Inc.

3. In at least 26 cases, the cautery or flame was present in or near the head, neck, chest, and respiratory tract of the patient and in all of the other cases the cautery or flame was incorrectly or inadequately protected from contact with a combustible agent.

4. In no instance was there a really closed circuit of administration although in several instances there were attempts to secure complete rebreathing for cauterization about the head, and the anesthetists involved believed the circuits to be tightly closed.

5. Tabulation of the 55 cases presented in this report clearly shows the truth of the following statements:

a. Explosions and fires of *all* combustible anesthetic agents and mixtures are capable of causing death.

b. Explosions of ether-air mixtures are capable of causing death.

c. Ether-air mixtures have a relatively small tendency toward propagating a wave of flame or pressure into and down the respiratory tract.

d. Ether-oxygen, with or without nitrous oxide, has the same great tendency toward propagating a wave of flame or pressure through the respiratory tract as has ethylene-oxygen and cyclopropane-oxygen when compared under similar clinical circumstances, i.e., the location of the point of ignition with reference to the respiratory tract of the patient.

e. In no case of which we have satisfactory knowledge has anyone been killed when the cautery or flame was present outside of a 12 inch zone surrounding the upper respiratory tract. This is just as true of ethylene as it is of ether. The large admixture of air (79 per cent nitrogen) which is inevitable when the inhalant anesthetic is ignited at a distance of 12 inches or more markedly diminishes the great explosive force and propagation tendency of combustible mixtures containing high oxygen percentages.

f. All deaths—and all were patients—have been the result of a flame or cautery employed within a 12-inch danger zone surrounding the upper respiratory tract.

6. The Flagg test for the determination of the combustible nature of the atmosphere over or in a proposed field of use of the cautery has been described and recommended.

7. A set of rules for the use of the cautery in relation to combustible anesthetics has been outlined and proposed for the standardization of safe practice.

8. If the cautery must be used in or near the head, neck, shoulders, chest, and proximal parts of the upper extremities, the anesthetic agent must be noncombustible.

9. If the cautery must be used in other parts of the body or operating room the anesthetic agent of choice should be noncombustible. If it must be combustible then the safeguards described should be followed to the smallest detail.

10. The cause of anesthetic explosions and fires when ignited by a cautery or flame is ignorance or carelessness. The prevention depends entirely on education and the elevation of the standards of anesthetic training and practice.

[1] We have just learned of 2 more cases, never reported before, in which the patients were seriously burned as a result of anesthetic combustions caused by a cautery used during an ethyl chloride spray and a nitrous oxide oxygen ether anesthesia for neck carbuncles.

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EDITORIALS

SURGERY
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FEBRUARY, 1942

RESECTION FOR CARCINOMA OF ESOPHAGUS

THE progress that has been made in the operative treatment of carcinoma of the esophagus and of the cardiac end of stomach involving esophagus represents one of the most rapid and striking contributions to surgery in the past four or five years. For about thirty years previously numerous attempts had been made at resection of the esophagus. The percentage of survivals following operation, however, was small and early recurrence was the rule, although the first case to be successfully resected by Torek in 1913 was free from recurrences at the time of death thirteen years later. In 1938 Garlock reported three survivals following thoracocervical resection and Marshall and Adams and the writer reported one case each of survival following transthoracic resection and esophagogastrostomy. Then began a sharp improvement in results, and a veritable wave of operating is now sweeping over the surgical centers of the country. That the undertaking is a justifiable one is indicated by the reports of the *Transactions of the American Association for Thoracic Surgery* for 1941 and of Garlock.

The advancement has come about as a result of better anesthesia, better control of intrapulmonary pressure, more liberal use of blood transfusion for maintenance of the circulation and respiration, and better technique of esophagogastric anastomosis based partly on animal experiments and partly on experience in human operations.

Resection for carcinoma of the upper half of the intrathoracic esophagus may be performed through either the left chest after the method of Torek and Garlock or through the right chest after ligation of the vena azygos as advocated by Wookey. In either case the proximal portion of the esophagus is brought out through the neck and an esophagostomy established as low on the neck or chest as possible. If there is sufficient esophagus left at the lower end an esophagostomy is performed by making a short abdominal incision just below the xiphoid, passing a dressing forceps backward above the left lobe of the liver through the esophageal hiatus, grasping the pursestring suture of the esophageal stump and pulling it through to the surface. If inferior esophagostomy is impossible a large mushroom catheter gastrostomy may be performed. Reconstruction of the esophagus by a tube of skin from the front of the chest has been carried out by Wookey.

For operable carcinoma situated in the lower esophagus, left transthoracic resection followed by esophagogastrostomy is usually feasible, but, when approximation and anastomosis cannot be attained, the operation should

be carried out as for carcinoma situated at a higher level. Carcinoma of the cardiac end of the stomach may also be resected through the same approach and esophagogastrostomy performed. The left chest is opened preferably through the eighth rib bed, and the lower esophagus including the accompanying vagi, isolated. The phrenic nerve is pinched, and the diaphragm is opened back to the esophageal hiatus. The lesser curvature of the stomach is ligated off down to and including the gastric artery, and the greater curvature is freed to a variable extent depending on the situation of the carcinoma. If it is in the esophagus and high enough to permit, the esophagus is divided at the cardia and the distal end is invaginated; if it extends to the cardia the division is made through the adjacent stomach and the distal end turned in. If the tumor is primary in the cardiac end of the stomach, the greater curvature should be ligated off along at least its upper half and the spleen removed. The stomach is then transected well below the tumor and the distal cut end is closed. Anastomosis is then made whether after resection of lower esophagus only or of upper stomach and lower end of esophagus by approximation and suture of end of esophagus to side of stomach within the chest. The diaphragm is sutured about stomach and the chest wall is closed tightly with an intercostal mushroom catheter inserted for suction drainage.

The writer has had a personal experience with nine resections, six primary in the esophagus and three primary in the stomach. Of the six primary esophageal cases, four patients survived the operation and of the three primary gastric cases, two patients survived. Of the four cases of esophageal resection through the thorax and neck, one patient died eight days after operation, one is alive after seven months, and two died of recurrences ten and fourteen months, respectively, after operation. Of the five cases—two esophageal and three gastric—treated by resection and esophago-gastrostomy, one patient, an esophageal case, is alive and free from signs of recurrence three years and five months after operation and of two gastric cases both survived the operation but have been operated on too recently to judge about the likelihood of recurrence. One patient with esophageal and one with gastric resection died from local infection as a result of the operation.

There is every indication that transthoracic resection will soon become the recognized form of treatment for carcinoma of the thoracic esophagus and of the cardiac end of the stomach and with early diagnosis and early operation, the results should equal those obtained in surgery for carcinoma of many other regions of the body.

DALLAS B. PHEMISTER.

MYOMECTOMY

BECAUSE myomectomy is an inherently more difficult operation than hysterectomy, its performance by any but experienced gynecologists is often associated with a higher mortality. As a result, it is still generally believed to be the same dangerous operation which, like hysterectomy, it was when it was first introduced. As a further result, its present field of usefulness is deliberately limited, although actually, when comparative series are reported by the same competent surgeons, the mortality of myomectomy is no higher and is frequently lower than that of hysterectomy.

To justify its performance, the end-results of myomectomy must include anatomical restoration, symptomatic relief, and functional cure. To achieve these results, a very careful selection of cases is necessary.

The single myoma is the ideal type for myomectomy, although all types and combinations of types, including the submucous variety, can safely be removed. Although a hundred or more tumors have been successfully removed from the same uterus, hysterectomy in such circumstances would usually be the operation of choice. Subsequent childbearing being one of the prime objects of myomectomy, there is small point to the preservation of an organ the musculature of which is so damaged that pregnancy is unlikely to occur in it. Quite aside from the size and number of growths they frequently present, myomectomy is usually contraindicated in negro women because the high incidence of associated adnexal disease in this race militates against the functional result which is one of the aims of the operation. By similar reasoning, the location of myomas in the uterine horns is another contraindication to myomectomy. Pregnancy can occur after the removal of one tube and the opposite ovary, or even after such ordinarily undesirable procedures as bilateral resection of the ovaries, but the majority of gynecologists doubt that plastic procedures on the resected tube are ever of great value. Degenerative changes, being usually limited to the tumor itself, are not a contraindication.

The ideal age for the performance of myomectomy is from 25 to 38 years. Below that period fibroids seldom cause symptoms, and over it the preservation of function is not of great importance. The upper age limit may occasionally be exceeded if a single fibroid is found in an otherwise healthy pelvis, in the course of surgery for other conditions, or if the patient insists for some reason upon the preservation of the uterus.

If these various limitations are observed, myomectomy will be found applicable to perhaps 10 or 15 per cent of all the patients with uterine fibroids seen in private practice. Proportions as high as 25 to 50 per cent, which have been reported, suggest that the indications have been unduly exceeded. For economic or other reasons the operation is seldom possible or even desirable in patients seen in public institutions.

Recurrence of the tumors is a possibility in a small proportion of cases; 3 per cent is a conservative average, though higher percentages are occasionally reported. Recurrence is unlikely after the enucleation of large single tumors and most frequent after the removal of multiple small "seedling" tumors, for which, except for special reasons, myomectomy is not usually a very wise choice. The patient for whom myomectomy is proposed should always be warned of the possibility of recurrence, but may, with equal fairness, be told that it is unlikely.

Anatomical restoration of the uterus can usually be anticipated, the process of involution reducing it to normal size and shape within 2 or 3 months after operation, even when immediately afterward it is large and its contour is irregular. Symptomatic relief, that is the correction of dysmenorrhea and the return of the periods to normal in character, frequency, and amount of flow, can be looked for within the same length of time in 80 per cent or more of all cases.

Myomectomy should not be undertaken for the relief of sterility until the problem has been surveyed from every possible angle, and the candidate for operation should understand that no definite promises can be made as to results. The reported successes, however, run as high as 33.3 per cent when the basis of computation is the number of suitable subjects, and when due allowance is made for the not inconsiderable number of women who frankly do not desire children. Subsequent pregnancies are associated with no

higher percentage of malpositions and dystocias than occur in other pregnancies in the same age groups, and cesarean section need be performed only on absolute indications, since the myomectomy scar is somewhat less liable to rupture than the cesarean section scar.

Attention to certain technical considerations simplifies the operation and makes it more likely to produce the desired results. Preliminary curettage should be carried out routinely, to remove polyps, identify possible submucous fibroids, and rule out possible malignant processes. Absolute hemostasis is essential. It can be secured by a variety of simple devices, such as preliminary control of the uterine blood supply, and the placing of additional sutures half an inch beyond each end of each individual incision into the uterus. Care should be taken that sutures are not tied tightly enough to blanche the tissues, which would lead to ischemia and sloughing.

Judgment is required to determine whether multiple incisions or the removal of several fibroids through a single strategically placed incision is the wiser. Incisions on the posterior uterine wall should be avoided whenever possible, and careful peritonealization should be carried out if they must be employed. There is almost no contraindication to the opening of the uterine cavity, even during pregnancy, when, if complications should develop, myomectomy can usually be performed without disturbance of the gestation.

There can be no quarrel with Victor Bonney's statement that since cure without deformity or loss of function must ever be surgery's highest ideal, myomectomy is a higher surgical achievement than hysterectomy. Myomectomy is not, however, an operation for the inexperienced gynecologist, if for no other reason than that there is no standardized technique for its performance, as there is for hysterectomy, and the method of procedure therefore depends upon the exigencies of the individual case. Naturally, this is no contraindication to myomectomy. The patient's indisputable right to the best possible treatment for her special trouble should not be dependent upon the inability of her gynecologist to perform a certain operation because it is difficult, or his ability to perform one operation, particularly one which is mutilating in its results, better than he can perform another, particularly another operation which preserves function.

HILLIARD EVE MILLER.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE excellent comprehensive book *Radiologic Physics*[1] is an outgrowth from the authors' experience in teaching the radiation courses at the University of Pennsylvania. At first glance the text appears formidable, but a further study shows that the mathematical considerations have been reduced to a minimum and proceed from elementary considerations into the more advanced material. Basic and fundamental information in theoretical and applied electrical engineering and radiation physics is treated in a simple, clear, and accurate manner. The book is divided into two parts. The first part consists of a discussion of the theory and practice of electrical engineering as applied to radiological apparatus. The second part deals with the theory and application of x-ray physics to x-ray diagnosis and therapy and to γ-ray therapy. To aid the reader in the mathematical consideration the authors have added an appendix which consists of a discussion of elementary trigonometry and calculus. This book is carefully organized so that it leads the beginner with very little knowledge of mathematics or physics to a firm foundation in the fundamentals of radiologic physics. There has been a real need for a textbook covering these phases of radiology. This volume deserves wide distribution and represents the most thorough discussion of radiologic physics available. It will be of particular interest to radiologists, teachers and students of radiology, but should be of interest to any physician who is interested in the use of electromedical equipment. EARL E. BARTH.

AS supervising editor of the *Supplement of The Practitioner's Library of Medicine and Surgery*[2], Dr. George Blumer states, "There is probably no subject in which change takes place more rapidly than it does in medicine. . . . The publishers feel in presenting this supplement that it covers important new work and brings up to date the entire system."

The first chapter on psychosomatic medicine is followed by one on neutron rays and artificial radioactivity by the recent Nobel Prize winner, John Lawrence. Full sections on chemotherapy and the vitamins are discussed in relation to their various forms by well known authors. Equine encephalitis, torulus, rickettiosis, pneumonia, and pneumonitis are discussed, as well as less familiar diseases such as Bejel and Letterer-Siwe's disease.

Some sections are weak, largely because the subject is weak. The sections on therapy are well discussed; serum therapy in pneumonia, the use of vitamin K, sex hormones, dental caries, surgical relief of pain, surgery of patent ductus arteriosus are a few examples. The timely sections on the drug treatment of mental states and the chemistry and treatment of hypoparathyroidism are sections especially well handled. Many young authors are selected because of their subject interest. On the whole, I think this supplement is very well done.

M. HERBERT BARKER.

THE second edition of *The Management of Obstetric Difficulties*[3] by Paul Titus has been enlarged by the addition of 75 new illustrations and 82 pages of text. The chapter on the causes and treatment of sterility is complete, well illustrated, and of much practical value. Sulfanilamide and other new medical agents are discussed in the treatment of sepsis.

Old and modern classifications of deformed pelves are given, and the technique of x-ray pelvimetry by the methods of Thoms and Caldwell and Maloy are described in detail. The practical viewpoint of the author is indicated by his recognition of the necessity of considering the size of the fetal head in the problem of the diagnosis of cephalopelvic disproportion. Apparently, however, he is not familiar with the usefulness and wide application of the simple method of measuring the pelvis with the head. The procedures recommended, with which there might be disagreement, are few and mostly unimportant. In such a practical book, however, the danger of extraction of the breech before the cervix is dilated, following Braxton Hicks' version, should at least have been mentioned if not emphasized.

The text is well illustrated and includes a number of colored plates, one of which is an excellent picture of a positive pregnancy test in a rabbit.

This text is the kind of book to which a doctor can turn for good advice on any obstetrical problem. The author avoids the discussion of controversial points and, on the basis of a generally sound obstetrical doctrine, gives the methods he has selected to be used in each condition. The man in general practice will find the book of much practical use for reference in any obstetric difficulty and a valuable addition to his library. DAVID S. HILLIS.

THE popular book *Roentgen Interpretation*[4] by Holmes and Ruggles has long since established itself as an excellent textbook for undergraduates. The fact that this is the sixth edition of this volume

[1] RADIOLOGIC PHYSICS. By Charles Weyl, S. Reid Warren, Jr., and Dallett B. O'Neill. With a foreword by Eugene P. Pendergrass, M.D. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1941.

[2] THE PRACTITIONER'S LIBRARY OF MEDICINE AND SURGERY, 1940 Supplement. New York and London: D. Appleton-Century Co., 1941.

[3] THE MANAGEMENT OF OBSTETRIC DIFFICULTIES. By Paul Titus, M.D. 2d ed. St. Louis: The C. V. Mosby Co., 1940.

[4] ROENTGEN INTERPRETATION. By George W. Holmes, M.D., and Howard E. Ruggles, M.D. 6th ed. Philadelphia: Lea & Febiger, 1941.

is a testimonial to its worth. It is unfortunate that one of the authors, Dr. Howard Ruggles, whose untimely death occurred on December 29, 1939, could not help in the preparation of this sixth edition.

The general character of the book has not been changed nor has any attempt been made to cover the entire subject completely. The subject material is presented in a concise but adequate manner and covers the entire field of roentgen diagnosis. The more recent advances in roentgen interpretation have been described and illustrated. In many instances illustrations have been replaced and new ones have been added. The only possible criticism that one could make is that the illustrations are in the positive rather than in the negative phase. This book is recommended without reservation as a text for undergraduate students, to postgraduate students in radiology, and to the medical practitioner.

EARL E. BARTH.

THE third edition of Kolmer and Boerner's *Approved Laboratory Technic*[1] is practically the same as the second edition except for the addition at the end of the book of an appendix of the newer methods developed in the last few years. These methods include the Donath-Landsteiner test for paroxysmal hemoglobinuria; Quick's method for quantitative determination of prothrombin; methods for the examination of semen; Sparkman's methods for urobilinogen in feces and urine used as a liver function test; Quick's method for hippuric acid in urine for liver function; Cherry and Crandall's method for serum lipase for pancreatic disease; a simplified Kolmer complement fixation test to be used in laboratories doing large numbers of tests for syphilis; the Eagle modification of the Wassermann test; a modified Medes method for vitamin C in urine and the Farmer and Abt method for plasma; the Bratton and Marshall methods for sulfanilamide in blood and urine, and sulfathiazole in blood; the bedside method of Ratish and Bullowa for sulfapyridine in blood; and Barker's method for thiocyanates in blood. The only changes in the main portion of the text from the last edition are the correction of errors and the addition of two tables: one, on page 314, is by Merritt and Fremont-Smith comparing normal cerebrospinal fluid with blood plasma; the other, on page 379, tabulates the color changes of the indicators of Clark, Lubs, and Cohen.

In most instances only one method is enumerated for each test, on the whole these are adequate. A uniform method of presentation of each test is conformed to throughout the book. The principle of the test is stated first, then the technique is given in outline form making it easy to follow. A praiseworthy feature in many of the procedures is the statement of the sources of error. A large number of the methods have a brief discussion of the interpretation or significance of the results of the test. However, this is not adequate to make this volume valuable as a textbook for medical students.

The authors have been assisted by 28 collaborators, all of whom are outstanding in their particular field.

This excellent volume on laboratory technique has been brought up to date by the addition of all the important new tests. It excels particularly in the two sections devoted to bacteriological, mycological and parasitological methods and serological methods. These two sections comprise 372 of the 870 pages. There are 380 figures in black and white and 12 colored plates. Fifty pages of index make reference easy. As a laboratory guide and reference book, it should be available to every clinical pathologist and laboratory technician.

OPAL HEPLER.

SINCE there is no preface or foreword to *Fractures* by George Perkins[2], it is difficult to estimate the scope of the author's purpose. This book is a comparatively small one of 381 pages with a brief and perhaps inadequate index. It is written in a crisp, staccato style, and is almost outline in form. The illustrations are for the most part stippled line drawings, giving an elementary appearance far too diagrammatic to be useful to the student, as they in no way depict the contiguous soft parts which so often play a leading rôle in the management of fractures.

In many instances there are incomplete pages and the work as a whole cannot be taken as a good example of the bookmaker's art. It is entirely possible that this is due to the conditions under which it was published in London, 1940.

This book cannot be recommended for either student or practitioner as a textbook on fractures. It is essentially a handbook and will answer in a cursory way most fracture problems. Reading the book is analogous to attending a concentrated refresher course in fractures, and, as such, it may prove a useful adjunct to libraries of practitioners who may not have the time or facilities to go more deeply into a given subject in this field.

J. K. STACK.

THE book by Griffith and Mitchell, *The Diseases of Infants and Children* has been revised and published under the title, *Textbook of Pediatrics*.[3] The authors have condensed and attempted to simplify the book so as to be more valuable for student use. The revised book is a compilation of the knowledge of over 60 authorities in various fields. However, in order to retain uniformity throughout the book, the authors have written the entire work, holding closely to their plan of condensation and readability.

Under the section on growth and development it is good to note that a knowledge of normal variations is stressed. This is especially valuable in pediatrics, a field in which preventive medicine is predominantly practiced.

[1] APPROVED LABORATORY TECHNIC; CLINICAL PATHOLOGICAL, BACTERIOLOGICAL, MYCOLOGICAL, PARASITOLOGICAL, SEROLOGICAL, BIOCHEMICAL AND HISTOLOGICAL. By John A. Kolmer, M.S., M.D., Dr. P.H., Sc.D., LL.D., L.H.D., F.A.C.P., and Fred Boerner, V.M.D. 3d ed. New York: D. Appleton-Century Co., Inc., 1941.

[2] FRACTURES. By George Perkins, M.C., M.Ch. (Oxon.), F.R.C.S. London and New York: Oxford University Press, 1940.

[3] TEXTBOOK OF PEDIATRICS. By J. P. Crozer Griffith, M.D., Ph.D., and A. Graeme Mitchell, M.D. 3d ed. Philadelphia and London: W. B. Saunders Co., 1941.

Many of the changes and reorganization in this book were necessitated by recent and newer knowledge. For example, the chapter on vitamins is briefly summarized and brought up to date. The chapter on endocrinology has been modernized. The discussion of the thymus gland is shortened and made more clear and concise. The same change has been made in the discussion of the adrenal gland. The section on treatment gives a brief but usable dissertation on the new drugs and their uses.

Several new chapters have been added. There is a section on pediatric institutions and organizations. This chapter is short and may give the student and beginner an insight into hospital organization. If so, it has served its purpose.

Following the section on physical growth and development is a new chapter on mental and emotional development. This section correlates the mental and emotional development with the physical and environmental factors.

It can be said without reservation that the authors in this instance have far surpassed their former efforts in forming a "Textbook of Pediatrics."

L. Martin Hardy.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

About Ourselves; A Survey of Human Nature from the Zoological Viewpoint. By James G. Needham. Lancaster, Pennsylvania: The Jaques Cattell Press, 1941.

Epilepsy and Cerebral Localization; A Study of the Mechanism, Treatment and Prevention of Epileptic Seizures. By Wilder Penfield, Litt.B., M.D. (Johns Hopkins), D.Sc. (Oxon., Princeton), and Theodore C. Erickson, M.A., M.Sc., M.D. (Minnesota), Ph.D. (McGill). Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1941.

Physical Medicine; The Employment of Physical Agents for Diagnosis and Therapy. By Frank H. Krusen, M.D., F.A.C.P. Philadelphia and London: W. B. Saunders Co., 1941.

Symptoms in Diagnosis. By Jonathan Campbell Meakins, M.D., LL.D. Boston: Little, Brown and Co., 1941.

The Microbe's Challenge. By Frederick Eberson, Ph.D., M.D. Lancaster, Pennsylvania: The Jaques Cattell Press, 1941.

The Modern Treatment of Syphilis. By Joseph Earle Moore, M.D. 2d ed. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1941.

Preeclamptic and Eclamptic Toxemia of Pregnancy. By Lewis Dexter, A.B., M.D., and Soma Weiss, A.B., M.D. Boston: Little, Brown and Co., 1941.

The Autonomic Nervous System; Anatomy, Physiology, and Surgical Application. By James C. White, M.D., and Reginald H. Smithwick, M.D. 2d ed. New York: The Macmillan Co., 1941.

Diseases of Women. By Harry Sturgeon Crossen, M.D., F.A.C.S., and Robert James Crossen, A.B., M.D. 9th ed. St. Louis: The C. V. Mosby Co., 1941.

Roentgen Diagnosis of the Extremities and Spine. By Albert B. Ferguson, M.D. Annals of Roentgenology, Vol. 17. New York: Paul B. Hoeber, Inc., 1941.

Gynecology and Female Endocrinology. By Emil Novak, A.B., M.D., D.Sc. (Hon. Dublin), F.A.C.S. Boston: Little, Brown & Co., 1941.

Gynaecological Operations. By J. Lyle Cameron, M.D., F.R.C.S. (Eng.), F.A.C.S., M.R.C.O.G. London: Humphrey Milford (Oxford University Press), 1941.

Subacute Bacterial Endocarditis. By Emanuel Libman, M.D., and Charles K. Friedberg. London, New York and Toronto: Oxford University Press, 1941.

Workmen's Compensation and the Physician; A Manual for the Use of General Practitioners and Insurance Carriers. By Henry H. Jordan, M.D. London, New York: Oxford University Press, 1941.

Perineopelvic Anatomy; From the Proctologist's Viewpoint. By R. V. Gorsch, A.B., M.D., New York: The Tilghman Co , 1941.

Blood Disorders in Children. By I. Newton Kugelmass, M.D., Ph.D., Sc.D. Spéc. London, New York and Toronto: Oxford University Press, 1941.

A Handbook of Midwifery; For Pupil-Midwives, Midwives, and Obstetric Dressers. By Sir Comyns Berkeley, M.A., M.C., M.D., Cantab., F.R.C.P. Lond., F.R.C.S. Eng., M.M.S.A. (Hon.), F.R.C.O.G. 11th ed. London, Toronto, Melbourne and Sydney: Cassell & Co., Ltd., 1941.

Synopsis of Genitourinary Diseases. By Austin I. Dodson, M.D., F.A.C.S. 3rd ed. St. Louis: The C. V. Mosby Co., 1941.

The Toxemias of Pregnancy. By William J. Dieckmann, M.D. St. Louis: The C. V. Mosby Co., 1941.

Surgical Practice of the Lahey Clinic, Boston, Massachusetts. Philadelphia and London: W. B. Saunders Co., 1941.

Diagnostic Roentgenology. Edited by Ross Golden. 1941 Renewal Pages. Vols. I and II. New York and Edinburgh: Thomas Nelson and Sons, 1941.

Our Sex Life; A Guide and Counsellor for Everyone. By Fritz Kahn, M.D. 2nd rev. ed. New York: Alfred A. Knopf, 1942.

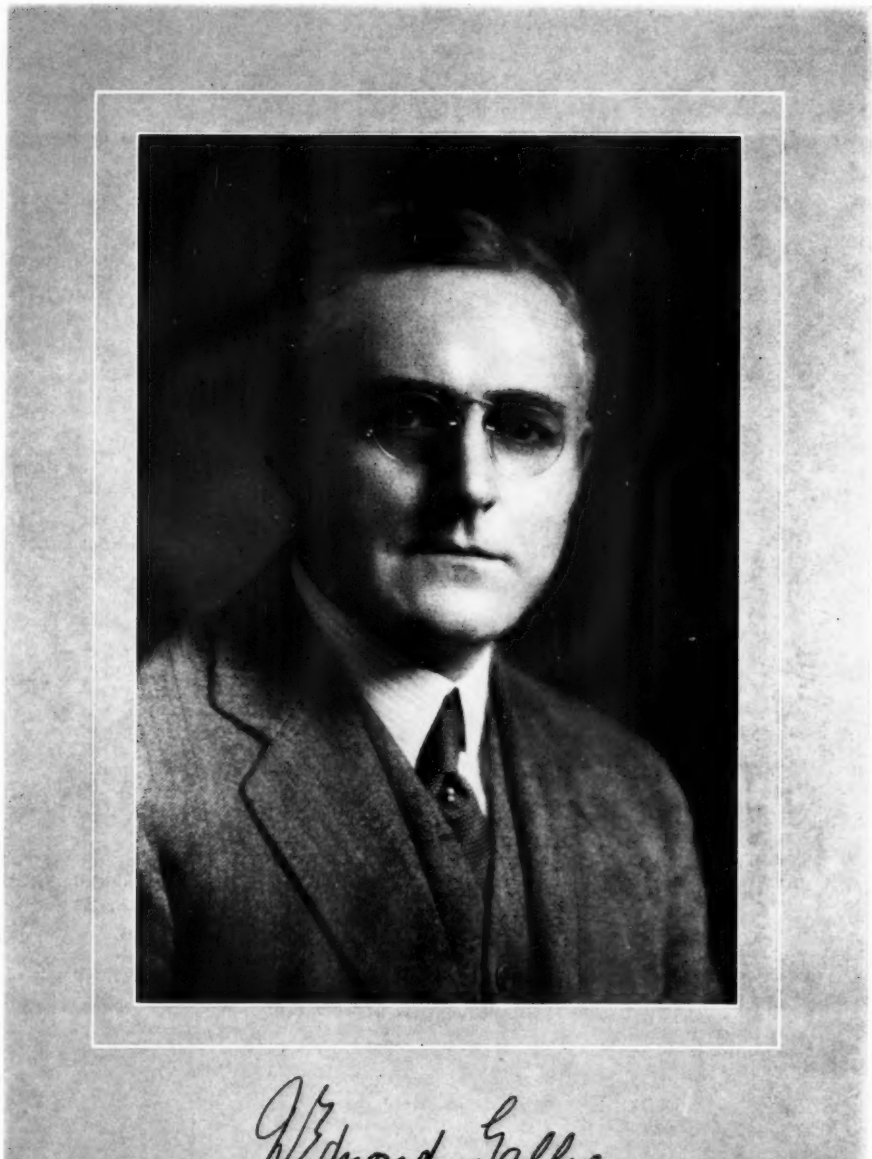
The 1941 Year Book of Pathology and Immunology. Pathology edited by Howard T. Karsner, M.D.; Immunology edited by Sanford B. Hooker, A.M., M.D. Chicago: The Year Book Publishers, Inc., 1941.

Surgery of Modern Warfare. Edited by Hamilton Bailey, F.R.C.S. Vol. 2. Baltimore: The Williams and Wilkins Co., 1941.

The 1941 Year Book of Industrial and Orthopedic Surgery. Edited by Charles F. Painter, M.D. Chicago: The Year Book Publishers, Inc., 1941.

Endotracheal Anaesthesia. By Noel A. Gillespie, D.M., B.Ch., M.A. (Oxon.), D.A. (R.C.S. Eng.). Madison, Wisconsin: The University of Wisconsin Press, 1941.

The Doctors Mayo. By Helen Clapesattle. Minneapolis: The University of Minnesota Press, 1941.



J. Edward Gallie

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AMERICAN SURGERY IN A CHANGING WORLD

EVARTS A. GRAHAM, M.D., F.A.C.S., St. Louis, Missouri

IN the slow, painful progress of human culture and advancement there have been frequent interludes in which this movement has been stopped temporarily by the catastrophe of war. For a thousand years, however, no threat of an extinction of culture and of the finer qualities of our civilization has arisen equal to that which exists now in the appalling possibility of a victory of Hitler and of his Nazi barbarians. It seems fitting, therefore, that at the meeting this year of this great body of surgeons we should consider soberly some of the consequences upon our profession which the war may have, particularly in order that by thinking of them now we may perhaps be better prepared to prevent their occurrence.

It is almost incredible that the Germany of only fifty years ago in which there originated much of the groundwork of modern science, including many of the important developments of surgery, should have degenerated into its present position of practical denial of the true values of intellectual enterprise.

The Nazi philosophy of the supremacy of brute force can hardly be reconciled with the fundamental ethical principle of attempting to help the weak and the underprivileged patient which has always been the basis, and, may I say the glory, of medical practice at least during the Christian era. Shirer,[1] in his *Berlin Diary* states that on May 6, 1940, Bernhard Rust, Nazi minister of education, said in a radio broadcast, "God created the world as a place for work and battle. Whoever doesn't understand the laws of life's battles will be counted out, as in the boxing ring. All the good things on this earth are trophy cups. The strong win them. The weak lose them." This authoritative statement from the man in charge of education in the Germany of today and possibly of continental Europe tomorrow, if taken at its face value, can mean only that in his opinion the purpose of education is to enable the strong to become stronger in order better to rob the weak. Surely that cannot be, some will say. It is unthinkable that anyone in a responsible position of authority could subscribe to so bestial a philosophy. But is not a sufficient answer to that complacent doubt to be found in what has already happened in the countries reduced to slavery—Poland, Czechoslovakia, Denmark, France, Norway?

Let anyone picture to himself the consequences if this conception of the ideals of education should dominate the world. In medicine no more humanitarian principles! Gone the charity hospitals! No more bother about crippled children! It is their own misfortune if the poor are sick and the children are crippled.

Presidential address of the retiring president, presented before the Clinical Congress of the American College of Surgeons, Boston, November 3–7, 1941.

[1]Shirer, William L. Berlin Diary, p. 328. New York: Alfred A. Knopf.

They are the weaklings. They "will be counted out, as in the boxing ring." What of the effect of the glorification of such brutality upon the doctor himself and especially upon the surgeon? Is such a philosophy compatible with the kind of surgical practice with which you and I are familiar? Certainly not. Why carry out all the troublesome details to make an operation as safe as possible? If the patient is strong he will recover anyway, and why worry if the weak does not survive? Doubtless the extreme results on the practice of surgery which I have just mentioned would not occur quickly but in the long run the corroding influence of a philosophy of brute force accepted by the dominant people of the European continent would be bound to degrade the present high standards which have been set up.

If then at the conclusion of this war Nazi influence should dominate the world a recurrence of the Dark Ages would seem to be inevitable so far as education and the progress of science is concerned. The spirit of the Spanish Inquisition would rear its ugly head again. Has it not already done so in those regions which have come under Hitler's control? The atmosphere of freedom necessary for the growth of science and the spread of education would not exist. German surgery since Hitler came to power has been practically sterile.

Those in America who, because of the wide expanse of the Atlantic Ocean feel secure against the possibility of a successful Nazi military invasion may think that it is of little concern to us here whether or not Europe adopts the Nazi ideology. But I cannot agree with that opinion. It is admitted probably by everybody that if Hitler is victorious in the European conflict it will be necessary for the United States to remain on a war footing indefinitely. This will mean not only a large army and navy but large taxes also. We have become accustomed to depend on private benefactions for much of the support of our universities and hospitals. It is common knowledge, frequently expressed, that already the reduction of private contributions has seriously handicapped many of our institutions. If those contributions become still less because of higher and higher taxes for the support of a huge preparedness program, radical changes in the whole scheme of higher education and of the support of scientific research will probably be necessary. It seems hardly possible that either education or research would be supported on the same generous scale if that support were dependent largely on government grants. Certainly much of the freedom to which we have long been accustomed in the privately supported institution would be curtailed with all the restraints, delays, and red tape necessitated by dealing with government clerks.

More important though might be the spread of the demoralizing Nazi theories of education to this side of the Atlantic which might be accepted under the impulse of necessity in competition even if they were considered undesirable. As long as three years ago reports from Germany indicated that the medical course had been shortened by a year and a half because of the demand for more medical officers in the Army. Is it inconceivable that such pressure might be made in this country for a shorter and "more practical" training if we are forced to stay indefinitely on a war basis? The close integration of the world which has been brought about by modern transportation and communication has made it difficult even for an educational system of one country to be uninfluenced by that of another strong and dominating nation.

That science knows no political boundaries is a common remark. An idea expressed in one country is elaborated in a second and built upon in a third to emerge as something practical and perhaps utilitarian. Great accomplishments are necessarily the products of many minds and hands. Surgical science in its development has been no exception to this rule. The evolution of modern surgery has been the work of all the enlightened peoples of the world, and the chief contributions to it have been made by those who have lived in atmospheres of the greatest intellectual freedom. If Europe continues to live in slavery and the rest of the world becomes an armed camp there will be little prospect of any notable advance in any of the sciences or cultural activities even on this side of the Atlantic.

At a time like this when international hatreds are strongly aroused it is well to recall some of the epoch-making contributions which

have served to create our modern surgery. Although it is difficult, if not impossible, to date the beginning of any great movement, to say who actually started it, it seems reasonable to state that the birth of the modern scientific spirit of surgery can be traced more definitely to the immortal Englishman, John Hunter, than to any other individual. Before his time, and for that matter during his life (1729–1793), there was no experimental approach to surgical problems and no accurate knowledge of the pathological conditions present. Surgical operations for the most part consisted of amputations, the opening of abscesses, and the removal of superficial tumors. Hunter, however, by his resort to the experimental method, his careful study of pathological specimens, his observations on comparative anatomy and on embryology established a scientific basis without which the surgery of the present day could not have developed. While Hunter was inaugurating the new sciences of experimental pathology and experimental surgery in England the army surgeon in Germany, according to Garrison, was still being called *Feldscherer*, because it was his duty to shave the officers.

To Great Britain, of course, also must go the credit of creating the antiseptic principle in surgery, carried to a revolutionary success by Lister, but later modified by the German, von Bergmann, into the technique of the present day asepsis. Lister's discovery, as everyone knows, made it possible for the first time to perform an operation on a patient without the previous fear of wound infection. The tremendous practical value of that work is likely to overshadow its other aspects. To me, however, some of those other aspects are of the greatest importance. Lister was a man of the same mental stripe as John Hunter. He was both a logical thinker and an experimentalist. From experiments which ran over a period of about twelve years he reached certain tantalizing conclusions about the nature of wound infection but he was unable to go further on his own knowledge. For example he had concluded that: (1) putrefaction caused suppuration, and wound infection did not occur without suppuration; (2) suppuration (decomposition) was in some manner caused by the presence of air; (3) the gases in the air were not responsible. What could it be in the air that was responsible, if not the gases? In 1865 his colleague at the University of Glasgow, Dr. Thomas Anderson, the professor of chemistry, called his attention to the papers of Pasteur on fermentation and putrefaction. Now he found the answer to his question. This to my mind is a splendid example not only of the interdependence of one nation upon another in science but of the interdependence of one science upon another. Was it not a revolutionary idea in itself at the time that a surgeon could receive help from a chemist on a "practical" problem like the healing of a wound?

Another major British contribution to the development of modern surgery has been the part played by the trained nurse. It seems doubtful to me that the art of surgery could have reached its present high plane without the sympathetic devotion to the patient and the careful attention to details which can be given only by intelligent women. The fact that Florence Nightingale and Joseph Lister were contemporaries has been of the greatest importance to us.

Germany through the influence of its great universities on medicine during especially the latter half of the nineteenth century and in the present century until the World War did much to extend the development of the scientific spirit in surgery. The older members of this audience will recall how eagerly the German surgical journals were read before the World War to learn of the latest developments in both the art and science of our profession and with what authority we at least in this country considered the German masters to speak. In looking back now, however, to the period nearly thirty years ago when German surgery was at its peak it would seem that what inspired us and fascinated us most was the spirit of scientific inquiry which was developed in that country to a greater degree than in any other up to that time. The best German university surgical clinics were centers of experimental investigation and were influenced by, at the same time as they themselves were influencing, other medical sciences, notably physiology and pathology. With the advent of antiseptic and aseptic surgery the German and

Austrian surgeons seized eagerly upon the opportunity to extend the occasional previous attempts to explore the possibilities of abdominal surgery. As a result particularly of the work of Billroth and his distinguished pupils, notably Mikulicz, Czerny, Woelfler, Gersuny, and von Eiselsberg, visceral surgery was added to the field of the surgery of the extremities. Billroth, however, made another important contribution, namely, a plan to educate young men to be surgeons comparable to or even to excel the "chief." It seems strange to us that the idea was so late in being proposed. Yet outside of the German and Austrian universities it was slow to take root. Even the great Lister had no disciples of the sort who were trained and developed in the well known surgical clinics of Germany and Austria.

In spite of the development of the science of surgery to a high degree in Germany, no individual giants arose comparable in stature to John Hunter or Lister. Contributions of others who were not surgeons, however, did greatly influence the science and art of surgery perhaps as profoundly as those of Hunter and Lister. I refer especially to the contribution of the x-ray by Roentgen and to the development of the new bacteriology by Robert Koch.

The United States has had an important share in the development of modern surgery. It is customary to say that our greatest contribution has been surgical anesthesia. There can be no question that this was of the first magnitude, ranking with Lister's antisepsis as one of the principal foundations upon which modern surgery was erected. Yet it seems to me there have been other American contributions almost, if not quite, as noteworthy, although less dramatic.

The elaboration of the nature of and the present treatment of surgical shock has been largely accomplished by Americans, although no single name in this connection stands out so prominently as with each of the other epochal discoveries previously mentioned. Until the beginning of this century only the haziest of ideas existed among the surgeons of the world as to the nature of this serious and frequent complication of severe injuries and of major operations. Crile's researches published in 1899, although not the first, and although later shown to be partly wrong in their conclusion, nevertheless focused the attention of surgeons on this subject and had great influence in arousing their interest. The more recent work of the American surgeons, Blalock, Phemister, Scudder, and others has added greatly to our knowledge of the fundamental mechanism of the production of shock. The contribution of Lewisohn of the harmlessness of the transfusion of citrated blood furnished a practical method for the better treatment of shock. The most recent development of using dried plasma instead of whole blood has been chiefly made by workers on this side of the Atlantic. The first experimental use of it for this purpose was by Bond and Wright of the University of Pennsylvania in 1938. As a result largely of the American contributions to this subject, a danger ever present in serious operations which is scarcely less important than that of infection has been practically banished from modern operating rooms.

As a sort of corollary to both the principles of the prevention of wound infection and the protection of the patient against surgical shock there stands the necessity of the gentle handling of tissues in order to accomplish a healing of the wound as nearly perfect as possible. To Halsted of Baltimore no less than to his Swiss contemporary, Kocher, belongs the credit of the passing of the rough and ready slapdash surgery which was prevalent a generation ago. Americans who had come under the influence of the careful, painstaking, deliberate, and almost bloodless operating technique of Halsted were usually amazed when visiting the well known German surgical clinics of the time to see the surgeons wearing rubber boots, the disregard of hemorrhage, the rough handling of the tissues, the careless closure of the wounds, and the shocking anesthesia. These sights usually made an indelible impression that the German surgeons, although perhaps greatly interested in the science of surgery, had failed to cultivate its art.

In order that the public may profit by developments in any science it is necessary of course that those developments should be

placed at the disposal of a large number of people. The important surgical advances which were rapidly developed after the advent of Listerism would have been of very little use to the general public if there had not been a considerable body of surgeons trained to make use of them. The system of training young surgeons put into effect by Halsted at the Johns Hopkins Hospital, the so called graded resident system, appeals to us Americans as being in principle the best method yet proposed. The fact that it is being used extensively in this country and elsewhere has been of incalculable value in raising the general level of surgical practice.

There must not only be well trained surgeons to carry the new developments of our profession to the public but there must also be facilities for the use of those developments. The United States and Canada have been leaders in the creation of a sort of hospital which until very recent years was unknown in those countries which followed European customs. The idea that the hospital is an institution for only the poor has been prevalent for centuries in Europe. As modern medicine developed, necessitating complicated apparatus and equipment for diagnosis and treatment, the remark was frequently made by our European colleagues that the middle class and the rich, who were taken care of either in their own homes or in the institutions known as nursing homes, were denied the medical care received by the poor. The North American idea, however, fortunately for us and for our patients, has been that a hospital could serve all classes in the community. Long ago surgeons here stopped performing major operations in the patient's homes except in isolated instances. There is no country in the world in which good hospital care is so readily available for all classes of patients as it is in the United States and Canada. But it was not always so. Some hospitals would like to cut corners by all sorts of economies which might make them unsafe for the surgical care of unsuspecting patients by even well trained surgeons. It is necessary to compel such institutions to live up to certain standards if they wish to maintain their good reputation with the public. The hospital standardization program carried out by the American College of Surgeons for nearly twenty-five years under the very able leadership of Dr. Malcolm MacEachern has been unique. No other organization in the world has performed the same function. Its influence in maintaining a high standard of surgical practice in North America has been incalculable. Perhaps it would be no exaggeration to say that the hospital standardization program has been no less powerful than the trained nurse in carrying the benefits of modern surgery to the general public.

My purpose in mentioning some of the outstanding developments which have created what we know as modern surgery has been to emphasize its internationality, rather than to attempt to give a brief historical review. I have, therefore, omitted many important discoveries and contributions which others might think deserve to be mentioned in a discussion of the parts which the leading countries of the world have had in establishing the science and art of our profession.

It is unthinkable that this structure so laboriously created should be destroyed, but to preserve it will almost certainly be the responsibility and obligation of those of us who live on this side of the Atlantic at least until such time as the world has recovered from the exhaustion which will follow the struggle for the crushing of Hitlerism. From force of circumstances the surgical world will surely look to America for leadership. We must be prepared to accept that responsibility.

Although surgery is international in its scope, its development in different countries has been characterized by differences of emphasis and by differences in point of view which have resulted in a more or less distinctive and characteristic quality of the surgery in the principal nations. Thus, for example, British surgery in many respects differs from our own and the German surgery. Likewise American surgery differs from the German. There is, of course, nothing surprising in this fact. Each of the three nations mentioned has a different culture and different traditions, and distinguishing features can be recognized in many intellectual activities, as in their methods of general education, in their music, their art, their architecture and so on.

Our own surgery more closely resembles that of the British than any other. The differences are somewhat intangible and difficult to describe; yet they are apparent. They can perhaps best be summarized by stating that we are more theoretical and less practically minded. We are a younger nation and, therefore, less conservative. The British surgeon is a master clinician in the application of the older art of physical examination to diagnosis and he is unexcelled in technical operative skill. He has carried on splendidly the tradition of anatomy as the foundation stone of surgery. We Americans, on the other hand, as a result of the changes in our undergraduate medical curriculum, have almost forsaken the gods of our fathers, anatomy and pathology. We have been seduced by the newer and more alluring gods of physiology and biochemistry. We have become more interested in function than in structure. It has been an amazing revelation to the American Board of Surgery to find that a generation of young surgeons has grown up whose ignorance of the anatomy and of the pathology of the structures with which they are dealing is abysmal. The wonder is that such men can be doing as good surgery as they undoubtedly are doing. Although the revelation shakes one's faith somewhat in the necessity of a sound knowledge of anatomy and pathology, nevertheless, it is difficult to believe that these same men would not be doing much better surgery if they did have sounder knowledge of those subjects.

It is probably an inevitable characteristic of a young rapidly developing nation to become ambitious to equal or to excel the accomplishments of older nations. The spirit of inquiry and of experimental research prevalent in the better German clinics before the First World War found favorable soil on this continent when it was transplanted here by many young men who saw in the rapidly developing sciences of physiology and chemistry many applications to clinical problems. It is not surprising, therefore, that the stream of publications appearing in the German journals had a profound influence on American surgeons. Moreover this influence came at a time when we in this country were most able to take advantage of it. From the beginning of this century on, more and more opportunities were presented to young men to undertake original experimental work. After the great awakening and the revolution in medical education which followed the publication of the Flexner report in 1910, together with the work of the Council on Medical Education of the American Medical Association, these opportunities were greatly multiplied. Experimental investigation and the spirit of scientific inquiry became glorified. The older, more drab and less fertile disciplines of anatomy and pathology became seemingly of less importance to the ambitious young surgeon. His desire was to startle the world with a new and important discovery. Not much chance of doing that in the intensively cultivated and exhausted soils of anatomy and pathology. The urge to get into print to make his name known obsessed every young surgeon who was ambitious to get along. Positions of prestige and influence were often filled on a basis of the candidate's publications more than on any other qualification. Sometimes the list would be regarded as more imposing if the number of the published articles exceeded those of the rival candidate, without a sufficient regard for their quality. Is it any wonder then that this urge for recognition resulted in a dimming of the lights of anatomy, pathology, and the old established methods of physical examination of the patient?

One of the American characteristics most frequently noted by foreigners is our tendency to undertake a new project or to accept a new idea with the utmost vigor and enthusiasm. Our acceptance of the value of the spirit of research in medicine was no exception. The movement in this country developed into a veritable surge, and large numbers of young men crowded into the research laboratories to find out something new. The printing presses were overworked to publish the volumes of work produced and scores of new medical journals appeared. There was little excuse for any Milton to be mute and inglorious. It was to be expected that most of the ambitious young investigators would be unfitted by nature to startle the world with any epoch-making discovery. On the other hand some, yes even some of the young surgeons, have

made very important fundamental contributions to our knowledge not only of physiology, both normal and abnormal, but even of pathology and of the forsaken subject anatomy, especially the anatomy of the nervous system. Others have added smaller stones to the building of our edifice. The spirit of research overflowed from this country into neighboring countries and back to Europe. With the benefactions of the Rockefeller Foundation distributed throughout the world there was scarcely a civilized country in which the spark of original investigation was not kindled into flame if it existed at all. Never before in the history of the world has there been anything remotely approaching the flood of scientific discoveries which has occurred in the last twenty years. Perhaps there will never be another period like it. In any case there is bound to be a recession of the wave. Almost certainly this recession has already begun. In all those parts of the world touched by the withering hand of Nazism research activities are impossible. England and Russia are handicapped by their struggle for existence. Only the nations of North and South America are so far free to carry on the spirit of research, and one wonders how long can this go on. Historians often have pointed out the wave-like character of the great cultural advances. During a relatively short period of time enormous progress is made, to be followed by a long period of relative inactivity or actual recession. Notable examples are the so-called Age of Pericles, the Alexandrian Period, and the Elizabethan Era. In view of the present chaotic conditions of the world, it would seem to require much optimism to assume that the period of unprecedented scientific advance through which we have just passed will continue with undiminished tempo.

Along with the recent period of enormous research activity there has been an immense improvement in the quality not only of the best but also of the average surgery practiced in this country. Better medical schools, more and better facilities for a long term specialized education of the young surgeon, more widely distributed well equipped hospitals have all had an incalculable effect in making good surgery available for the mass of the population. The high standards set for certification by the specialty boards have been a very stimulating influence in keeping the practice of the various surgical specialties on a high level. The development of group practice brought to a remarkable state of efficiency by the Mayo Clinic and emulated by many other clinics has also been a factor in improving surgical practice.

The influence of the American College of Surgeons has carried much weight in improving the average surgical practice throughout the country. Its splendid work in improving the hospitals of the United States and Canada has already been mentioned. Also important have been its recently increased standards of admission to fellowship, the work of its recently appointed committee on graduate education, its official journal, and its annual meetings where the surgeon out of touch with the medical centers of the country can come to learn of the new developments in surgery.

At the meeting this year an innovation in the program was made. The Forum on Fundamental Surgical Problems was created. This symposium of ninety short presentations of experimental work on surgical problems was arranged largely by the efforts of Dr. Owen H. Wangensteen. It can almost certainly be said without fear of denial that never before at any surgical meeting in any country has there been a program presenting so much original work, mostly by younger investigators. It constitutes, therefore, a unique event. Moreover, it represents, it seems to me, one of the chief characteristics of modern American surgery, the spirit of inquiry and the utilization of all the sciences for the solution of surgical problems. It is a characteristic of which we American surgeons can justifiably be proud. It removes surgery from the realm of mere craftsmanship and translates it into a science. It is this experimental attack which constitutes the front line of surgery. Does not this program show that the spirit of the immortal John Hunter still survives? His memorable words to Jenner should be recalled, "I think your solution is just; but why think? Why not try the experiment?"

In the foregoing remarks an attempt has been made to emphasize the fact that the de-

velopment of modern surgery has been due to important contributions from several nations but yet that the practice of surgery has certain national characteristics which make it different in different countries. Reasons have been advanced for assuming that the recent unprecedented period of scientific progress is certain to be checked, if it has not already been, regardless of the outcome of the war. A Nazi victory, however, will mean almost certainly for a time a more or less complete destruction of the scientific spirit throughout the world. It has been emphasized that attempts to preserve our present high standards and to carry forward the light of progress will fall most heavily on those of us who live in the Americas, South as well as North.

Let us now briefly consider some of the ways by which these standards can be preserved. I should say that it is of the utmost importance that the surgeons of North America and of Latin America come to know each other better and to develop a spirit of more sympathetic mutual understanding. The surgery that is being practiced in the centers of Latin America is not excelled anywhere, and an increasing volume of original work of very high order is being produced. The knowledge of this work has been only slowly diffused in North America because of difficulties in language. Likewise, for the same reason, our surgery has not been so well known to our southern neighbors as the continental surgery. Would not a regularly meeting Pan-American surgical congress with the cooperation of the American College of Surgeons provide a stimulating and helpful influence in preserving and fostering the spirit of surgical progress at least on this side of the Atlantic while Europe is recovering from the disaster of war? By meeting in different countries and at stated times, either annually or less often, there would certainly arise an inspiration from personal contact and from developing friendships and respects among those most actively engaged in the advance and practice of our profession. More of us North Americans would come to possess a knowledge of Spanish and Portuguese, and more of the South Americans, English. There would be a freer interchange of medical literature, of ideas, and of students. The American College of Surgeons already has a membership of 225 from Latin America. It could well be more nearly representative of all the Americas, both in membership and in its governing bodies, so that truly it would be an all embracing American College of Surgeons, thoroughly international in its point of view and administration. This suggestion may seem too radical, but we must be prepared to make radical moves if we wish to counteract the results of the swiftly moving tragedy in Europe.

In a discussion of the preservation of our highly developed modern surgery, it is necessary to touch upon our duties and obligations to the armed forces of our country in a program of preparedness for war. The Army particularly, and to a less extent the Navy, need more medical officers. We must do all in our power to provide them during the acute emergency. In striving to preserve our programs of training young surgeons we must not hamper the agencies of our government whose defeat would mean the destruction of our national independence. On the other hand, the armed forces should not unnecessarily and ruthlessly interfere with our laboriously developed system of training. Enough of it must be safeguarded to prevent too great a recession from our present standards. I am pleased to say here, to the credit of the wisdom of Surgeon General Magee of the Army and of Surgeon General McIntire of the Navy, that every effort has been made to interfere as little as possible with the training programs. Possibly a plan may be worked out whereby the young medical officers, after a limited service, can be released to finish their periods of training in the civilian hospitals.

Possibly greater dangers to the safety of our resident system will come from the governing bodies of our civilian hospitals when the specter of hard times leers at them. We must, however, hold fast to the principle of the system, even if some modifications become necessary. We must not forget that surgery is a science as well as an art and must constantly advance. Above all, to be true to our profession, we must remember that the practice of surgery is based on humanitarian principles. Come what may, we shall not subscribe to the philosophy of the supremacy of brute force.

ADRENAL CORTICAL TUMORS

The Types of Nonhormonal and Hormonal Tumors

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IN 1936, a study of adrenal cortical tumors was presented by a New York group from the Presbyterian Hospital. At that time it was shown that these tumors could be diagnosed by perirenal air insufflation. Attempts were also made to determine the hormones excreted in these cases. It was shown, that in adult females, normal or high amounts of estrogens were excreted in some tumor cases. At the same time Gallagher found that large amounts of androgens were present in the urine of 2 of the adult female cases but his report was not completed in time to be included in the published paper but was incorporated in the reprints. Since then the adrenal gland has been studied by numerous investigators and there has been a clearer understanding of many of its physiological activities. Coincidental with the advances in the knowledge of the function of the normal adrenal there has been much experimental and clinical investigation into its pathological status. Because of the better understanding of the clinical status with reference to adrenal cortical tumors, we believe that the report of a study of the adrenal cortical tumors which have been seen at the Squier Clinic is worthy of presentation.

THE ADRENAL

The mammalian adrenal is actually two glands fused together in development. Each has an essentially different origin, a different type of tissue and with a separate function, but they happen to be enclosed in one enveloping capsule and tissue stroma.

Tumors of the adrenal are not frequent. When they arise they can be basically classified as follows:

1. Tumors derived from the various layers of connective tissue, blood vessels, lymphatics, or nerve structures within the gland which are similar to such types of tumors that may occur in any other gland and as such are not peculiar to the adrenal. They occur very rarely in the adrenal. Tumors of these tissues having been reported as occurring in the adrenal are the following: fibroma, lipoma, neuroma, neurofibroma, myoma, osteoma, hemangioma, sarcoma, lymphangioma, and melanoma.

2. Tumors derived from the medulla are ones peculiar to that tissue and are of the ectodermal sympathetic nerve system. They may be of the basic nerve cell, a sympathoblastoma, or secondly from the sympathetic ganglion or ganglineuroma, or thirdly from the pheochromocytes or paragangliomas. The first two occur more frequently in children and are seen more often than the latter, which occurring mostly in adults are rare.

3. Tumors originating from the adrenal cortex are mesodermal glandular tumors, and cytologically are hyperplasias, adenomas, and carcinomas.

Accessory adrenals occur, called Marchand's bodies. These are of cortical tissue and have been described as in the kidney, the perirenal fascia, the retroperitoneal fascia, within the broad ligament, attached to the ovary, or associated with the gonadal testicular tissues. Tumors of these aberrant adrenals have been reported, all of cortical tumor type and, without and with, similar syndromes as are seen with adrenal cortical tumors. Their occurrence is very rare.

THE ADRENAL CORTEX

In a consideration of tumors of the adrenal cortex, it is essential to evaluate the more recent studies upon its embryology and briefly to review the marked advances of the knowledge concerning its biological processes.

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EMBRYOLOGY AND HISTOLOGY

The adrenal cortex originates from the mesoderm of the celom epithelium near the genital ridge and because of its proximity to that ridge, Grollman has suggested that cells of the latter may be included with the adrenal and that hyperfunction of these cells may be responsible for the phases of reproductive symptomatology in those cases. The cortex during postnatal life gradually forms into three microscopic layers that are completed to the adult cortex, at or about puberty. The development of the inner of these three layers just before puberty has been shown by Miller, Deansley, and Whitehead, to have some connection with the development at that time of the sexual glands and organs, and because of this it was suggested as an "X-Zone" of the adrenal. In this latter zone, because of his theory of inclusions in the juxtamedullary layer of testicular cells or rests, Grollman preferred to recognize a fourth zone or special "androgenic zone."

A better understanding of the development of the adrenal cortex has been furnished by the studies of Mulon, Bogmoloz, Goormaghligh, Hoerr, and Zwemer, in that the adrenal cortex apparently continuously grows from without inward. New cells are formed from the spindle-shaped fibroblastic cells underneath the fibrous capsule, develops through the three layers from without in, the zona glomerulosa, zona fasiculosa, and zona reticulosa and during this process elaborate, accumulate, and discharge lipoid sterols and then degenerating, are absorbed in the reticulosa near the medulla. The secretion is discharged into the capillaries by the mature cells before their degeneration and the process is constant, with replacement by new cells.

Under certain phases of hyperactivity there appear larger number of cells undergoing degeneration than is normally seen. This may suggest the possible reason for the widening of the "reticulate zone at puberty," (Deansley and Miller), the special zone (Grollman), and the appearance of granules in the cells with fuchsinophilic staining affinities as reported by Broster and Vines.

In relation to the appearance of discrete fuchsinophil granules found in certain adrenals in females manifesting virilism as reported by Broster and Vines, and Simpson and Joll, the recent report of Sudds is interesting. She found that granules are present in 24 per cent of adult male adrenals and 28 per cent of female adrenals. In females the percentage of glands with granules showed a steady increase with age. With the exception of 1 fetus, in no case under 24 years were they apparent. This report is an excellent investigation of a small number of such sections reported in our previous article (Cahill et al.) in which such granules were found in dogs, in adrenals of individuals without virilism and more marked in adrenal cortical tumors with virilism. Sudds concluded that age has some influence on the presence of these granules, but sex plays no part. By inference, from Sudds' conclusions, the presence of the increase of these granules in excess may be due to the aging influence of virilism when it occurs, and not that the granules were direct hormones which logically should be the sterols produced by the adrenal cells.

THE PHYSIOLOGY OF THE ADRENAL CORTEX

The adrenal cortex has been definitely established as the elaborator of hormonal substances, some of which are necessary for life maintenance. The hormonal substances have been shown chemically to be sterol lipoids.

Up to 1941 over 20 closely related sterol derivates have been prepared from the normal adrenal cortex. The action of all of these is not fully known. Of the identified steroids is one with the property of male sex hormone (dehydroisoandrosterone) (Reichstein) a beta kesteroid, that differs only in its chemical structure from the testicular male hormone (androsterone) an alpha kesteroid. There has also been identified as secreted by normal adrenals the female sex hormones, estrone (Beall), and progesterone (Beall and Reichstein). Thus normal adrenals have the power to produce both male and female sex hormones. The excretion in the urine of androgens is small in children, reaches a normal in adult life, and diminishes after 40. It is relatively small in females. Part of these androgens are considered to be derived from the adrenal. The excretion in the urine of estrogens also

occurs in small amounts in normal males, normal amount in normal females, and part of these estrogens are considered to be probably elaborated by the adrenals.

Some of the other steroids elaborated by the adrenal cortex have effects on the salt and water metabolism, the permeability of the capillaries, in the regulation of the carbohydrate, fat and protein metabolism, the renal function, the capacity of muscle response, and the resistance to stress. The maintenance of life and health is probably due to a combination of the various activities of these steroids. Of the identified steroids, one, desoxycorticosterone, seems to be most effective in the regulation of salt and water metabolism, in capillary permeability, and in preservation of renal function but has no demonstrable effects upon the carbohydrate metabolism. The properties of others of these steroids are not as yet clarified so that much further investigation apparently is necessary.

From the multitude of experiments reported there are suggestions that the adrenal may be implicated in many other metabolic processes. It has been shown that there is a relationship between the adrenal cortex and the gonal pituitary system and that hyperactivity of the ovary may partially replace adrenal function (Rogoff and Stewart, Emery and Schwabe). It is of interest to explain the presence in comparative large amounts of vitamin C in the adrenal cells as shown by Szent-Gyorgyi.

PATHOLOGICAL PHYSIOLOGY

Since the adrenal cortex is composed of hormonal secreting cells, there are periods of cell growth or degeneration in which these cells do not elaborate hormones. Hyperplasia of these cells or tumor of these cells will have large numbers of this stage of cell life present without increase of hormones delivered into the capillaries. Again hyperplasia or tumor of the cells in the various stages of elaborating and secreting the steroid hormones will have an abnormal number of these cells present and as a result the secretion into the capillaries of an excess of some or all of the various steroids. Such has been shown to be the result of hyperplasia or tumor in the adrenogenital syndrome in which the excess amount of male hormones

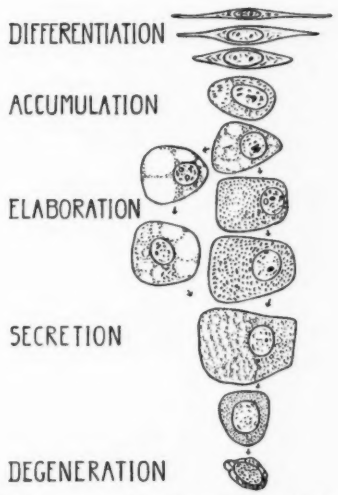

Fig. 1. Diagram taken from Zwemer of the development of adrenal cells, showing the differentiation of the long cells from the cortex into the glomerular zone, the fascilate zone and into the reticulate zone. During this process, they change, accumulate materials, elaborate substances, secrete them, degenerate, and are removed by macrophages and microphages near the medulla.

elaborated by the tumor has its effect upon the secondary sex organs. This has been shown to occur in the masculinization of females both children and adults and in the male maturity in male children (Simpson; Simpson, de Fremery, MacBeth; Gallagher; and Callow).

Hyperplasia or tumor cells at times have apparently elaborated excess amounts of steroids with female hormonal activity. The effect of these excess amounts of hormones may be registered upon the individual so affected. The feminism of a male has been shown to be the result of excess estrogens elaborated by a tumor of the adrenal cortex by Burrows et al., and by Simpson and Joll. There is then the suggestion that the presence of high amounts of estrogens as reported by Frank, from certain adrenal cortical tumors may naturally show no effect upon a female.

Bauer contends that an excess of the hormones which have the regulation of the electrolytes, salt and water metabolism, fat and sugar metabolism, are produced by the adrenal cortex either in the hyperplasia or in the tumors occurring in the syndrome described under many variations as Cushing's syn-

drome. This has been supported by the work of McQuarrie, Johnson, and Ziegler, and by Anderson and Haymaker.

It has been well established that the adrenals can elaborate androgens and estrogens as well as other metabolic hormonal sterols and there is suggestive evidence that the regulation of these secretions is subjected to, if not regulated by stimuli from the pituitary. These androgens and estrogens can be present in excess quantities and responsible for symptoms present. They may result from some aberration of normal cortical steroid metabolism or they may be just an increase of normal production. Evidence is present that with some tumors there may be abnormal steroids produced. From such is the report of Butler and Marrian of the steroid with male hormonal properties (pregnane 3, 17, 20 triol) associated with an adrenal tumor and they definitely established that such a hormone is not excreted by normal man or from a normal or pregnant woman.

In addition it has been shown by Butler and Marrian and by Venning, Weil, and Browne that some patients with virilism and adrenal hyperfunction excreted pregnandiol and believed that this originated from the cells of the pathological adrenal.

CLINICAL CLASSIFICATION OF TUMORS

Up to 1928 it was relatively rare for patients to be seen in the Presbyterian Hospital who suggested adrenal pathology, with the exception of the adrenal deficiency in Addison's disease. Since then, because of increased knowledge and interest in endocrine diseases, hundreds of patients with symptoms of supposed adrenal disturbance have been admitted to the Squier Clinic. From the large number examined, and the different investigations, the conclusion must be drawn that among adrenal syndromes the adrenal cortical tumor occurs infrequently. When it occurs it may be present without any evidence by symptoms that there is any change in the hormonal balance. In others it is accompanied by symptoms which are definitely due to hormonal influences. These symptoms vary according to the hormones secreted, their amount, and to the age and sex of the individual so afflicted.

The clinical groups, on the basis of proved cases may be classified as follows:

1. No recognizable hormonal changes
2. Changes due to excess androgens
   a. In female child toward adult masculinity
   b. In female adult toward masculinity
   c. In male child toward adult masculinity
3. Changes due to excess estrogens
   a. In adult male toward femininity
4. Changes due to excess androgens and other steroids
   a. Cushing's syndrome with associated sexual changes (mostly in females)
5. Changes due to excess other steroids related to metabolism
   a. Cushing's syndrome without sexual change (in male and female)

TUMORS WITH NO RECOGNIZABLE HORMONAL CHANGES

Tumors of the adrenal cortex have been reported in the literature as occurring without hormonal changes, (Hartung, Macera, Stevens, Gibson, Loeb, etc.). They are infrequent and have been seen practically only in adults over 30 and have occurred in both sexes. When discovered, they have apparently been present for a considerable period of time, first without any symptoms, but later with the complaint of pain in the side on which the tumor is present. Often when diagnosed the tumor was palpable. The deep situation of the adrenal and delay in invading any of the adjacent viscera for a considerable period before recognition, allows growth of the tumor often to a large size. The pain is both abdominal and flank, and usually is made worse by exercise. Symptoms of malaise, fatigue, and diminution of appetite are often present, especially in the larger tumors.

The following cases are illustrative of this type of tumor.

CASE 1. A.S., Chart No. 69341, Presbyterian Hospital (reported in 1936), a single woman, aged 38 years, was admitted in 1927 complaining of intestinal trouble and pain in the left side for over a year with occasional fever and weakness. She had missed her last menstrual period. She had a large mass in her left flank and cystoscopy showed that her left kidney was normal but was displaced downward by the mass. Her blood pressure was 155/68. There were no studies of urinary hormonal excretion. A transperitoneal operation removed a large tumor from above her left kidney. With the aid of a postoperative transfusion she made an uneventful recovery. Sec-

tions of the tumor showed a carcinoma of the cortex of the adrenal gland. In some areas there was a differentiation of the tumor with sections having arrangement of cells reminiscent in places of the different areas of the normal adrenal, the zona fasciculata, zona glomerulosa, and the zona reticularis. In other areas there was little or no such differentiation, but cells varying in size and shape and mitosis and infiltration. After 5 months' improvement there was recurrence of abdominal symptoms. While visiting in Nova Scotia she had an abdominal operation and a section of a liver metastasis was sent to us. This resembled the undifferentiated area of the original tumor. She was reported to have died 11 months after operation.

CASE 2. P.J.R., Chart No. 16156, Presbyterian Hospital (reported in 1936), a male, aged 58 years, was admitted in 1915 complaining of shortness of breath for a year, progressive loss of weight and strength, and blood tinged sputum. His right pleura was aspirated and the fluid contained epithelial tumor cells. At autopsy there was found a tumor of his right adrenal cortex with metastases to pericardium, endocardium, lungs, liver, kidneys, and retroperitoneal tissues. He had no hypertension, no fat deposits, no plasma, hair or secondary sexual changes.

CASE 3. S.S., Chart No. 360795, Presbyterian Hospital, a male, aged 36 years, married and with children, was admitted in 1936 with pain in the left loin and chest for over a year. He had had a double herniotomy, an appendectomy, a tonsillectomy, and a cholecystectomy in the several years before admission. His left loin pain was in periods lasting 4 to 5 days. There was some loss of sexual vigor and with his pain he often had headaches and thought that these came roughly once a month. He was a vigorous male with a well marked normal hair distribution and with normal male genitalia. There was no hypertension. Cystoscopy and pyelograms were normal except that the inner border of the upper pole of the left kidney seemed shadowed by some tissue. A perirenal air insufflation showed a rounded tumor above and anterior to his left kidney. A large soft adrenal tumor, anterior to the anterior capsule of his left kidney was removed with the kidney through a flank incision. The adrenal tumor capsule broke at the time of removal. After an uneventful recovery he was treated with high voltage x-ray. Urinary hormones estimated immediately after removal of the tumor showed a low excretion of both androgens and estrogens (male 4 I.U. and female 3 R.U. per day).

Sections of the tumor showed that there was an upper small portion of normal adrenal that blended into the neoplastic. In the tumor part, there were collections of cells of unusual size containing enormous nuclei. The cytoplasm was pale, pink, and smooth. Multiple nuclei were present. Mitoses were occasionally seen. In places the tumor cells were much smaller and resembled the renal hypernephromas. Cells containing lipoid vacuoles were not frequent. Areas of necrosis and hemorrhage were numerous.

Two years later the patient was readmitted with an abdominal mass which on transperitoneal exploration could not be removed because of its intimate attachment to the cava and aorta. Urinary hormones before operation showed male 15 international units and female 4 rat units, a low male excretion. High voltage x-ray was resumed. He was readmitted 6 months subsequent to this with symptoms of general peritonitis. He refused operation, died, and on autopsy a perforation of a sigmoid diverticulum with generalized peritonitis was found. There was a metastatic tumor involving his aortic glands and his vena cava. Although the vena cava was involved, no metastases were found in his lungs.

CASE 4. A portion of a tumor of the adrenal was sent to us by Dr. M. W. Roome of the Department of Surgery, University of Chicago. This was from a male adult who had a large adrenal cortical tumor without any hormonal changes. The operative procedure was corroborated by autopsy. The cellular pathology of Dr. Roome's tumor was somewhat similar to that of Case 3, although the very large cells and nuclei were not as frequent nor did they appear as large. Lipoid vacuolated cells were rare. Mitosis and infiltration were present.

CASE 5. A.K., Chart No. 652840, Presbyterian Hospital—Service of Dr. A. O. Whipple, a female, aged 50 years, single, was admitted September 1941 with loss of weight and strength for 8 months. Her history was negative except for menopause 12 years previously. Eight months before admission she began to have loss of appetite, weakness, and a gradual loss of 20 pounds. A mass then was seen to appear in her left upper abdomen without pain for the 4 months before admission. Because of a normal blood count and other tests it was thought to be a large spleen and was given x-ray treatments. With this and sunbaths she became darker in her skin. There was no increase in hair anywhere on her body, no changes in her breasts, and no headaches. She had no hypertension. From x-ray studies the mass was thought to be spleen. She was operated upon and a large tumor mass with dilated veins was removed. It was anterior and above the left kidney and was attached to but did not involve the kidney or the normal adrenal above. She made an uneventful recovery. Sections of the tumor showed cells resembling adrenal cells of the various types (similar to our Case 1). Cells with vacuoles were rare. The diagnosis was carcinoma of aberrant adrenal without hormonal symptoms.

Our 4 cases of adrenal cortical tumors, 2 males and 2 females, were all adults as was Dr. Roome's case. In each the tumor had been present for a considerable length of time and had reached a rather large size. Two presented symptoms of recurrent abdominal and flank pain on the side affected. All showed signs of malaise. One case was admitted in

the terminal stages and the symptoms were of lung metastasis. In 1 the mass was suspected to be of splenic origin and only at operation was it shown to be a tumor of an aberrant adrenal. In 1 case the diagnosis was made by the displacement of the kidney on pyelogram, and in another a perirenal insufflation x-ray film not only established the diagnosis but the fact that the tumor arose from the inferior portion of the adrenal and that it was mostly anterior to the kidney. Loeb recently reported making a similar diagnosis with perirenal insufflation roentgenograms upon a female of 48 without hormonal symptoms. A transperitoneal removal was successful and she, to time of reporting, had a survival period of 1½ years. Description of the microscopic sections of Loeb's cases resembled that of our 2 females. Sections of the male case curiously resembled each other and not those of the females. All the tumors were characterized in that cells with vacuoles of lipoids were very rare.

The prognosis of most nonhormonal cases has not been very good because of the lack of symptoms allowing the tumors to reach a large size before removal. Although all showed evidence of malignancy, some appeared slow to metastasize.

There was no evidence of acute adrenal deficiency following the removal of any of the tumors.

TUMORS WITH SYMPTOMS DUE TO EXCESS ANDROGENS

In the female child. The first case of tumor with symptoms due to excess androgens in modern literature was described by Thomas Cook in 1765. This was followed by Bevan and Romkild in 1802, Telesius in 1803, Ogle in 1865, and by Colcott, Fox, and Ogston. The occurrence of adrenal cortical tumors in female children naturally was early recorded because of the dramatic change towards male maturity. They are not frequent but form a considerable percentage of the recorded adrenal tumors.

When the disease occurs before birth or in early infancy in the female child the symptoms have been described as pseudohermaphroditism. Gallais theoretically thought that true hermaphroditism could occur if adrenal cortical tumor occurred early in fetal life. When pseudohermaphroditism occurs after birth a hypersecretion of the adrenal cortex, especially if due to tumor, may definitely be the cause of the syndrome. In these children all degrees of secondary sex anomalies are found from only a slight enlargement of the clitoris to an enormous size like a penis, accompanied by atresia or total absence of the vagina. The internal genital organs are usually small and sometimes deformed. There is often doubt about the true sex.

From the work of Ivy, Green, and their coworkers, it is strongly suggested that the syndrome of pseudohermaphroditism of very early infancy when not due to adrenal tumor or hypertrophy may be the result of the effect of hormonal activity in the mother upon the fetus during gestation.

The occurrence of female pseudohermaphroditism is not infrequent. We have studied 4 of these children, aged 3, 4, 5, and 9 years. The condition began early in life, with hypertrophy of the clitoris, with the appearance of hair upon the genitals, excessive body growth for awhile, increase in musculature, deepening in voice, accelerated epiphyseal and dental development, and a higher mental aptitude than their age. In all, androgens were demonstrated in the urine. Air insufflation roentgenograms showed in all a bilateral increase in the size of the adrenals. Complete operative explorations showed female internal organs, the biopsies of the ovaries showed no testicular inclusions, and section of some of the adrenals showed only apparent age acceleration in the adrenal zones and cells. These children have been observed over a period of several years, as yet without recognition of an adrenal tumor. All have had amputation of the penile clitoris, and after section of the adrenals the androgen output diminished.

That adrenal tumor can be the cause of such pseudosexual precocity is amply supported by cases in the literature. In a recent report Reilly, Lisser, and Hinman cite the case of a child of 22 months with pseudosexual precocity only, due to an adrenal cortical tumor, diagnosed by its effect upon the left kidney pyelogram. Microscopically it was a car-

cinoma of the adrenal cortex. They included a most thorough compilation of the literature of pseudosexual precocity, finding 40 cases, among which 2 definite tumors of the adrenal were successfully removed and 8 successful operations were performed for simple hyperplasia. They found 3 reported cases of successful removal of aberrant adrenal tissue tumors producing the same syndrome. None of these cases presented the other symptoms associated with the Cushing's syndrome. They found records of 10 patients in whom a tumor was present with the syndrome and who died during operation or within 3 days, 2 having some of the symptoms of Cushing's type. They also recorded 15 cases in which no operation was performed and in which an adrenal cortical tumor was found on autopsy. In 8 of these cases obesity, bloatedness, flabbiness, glycosuria, osteoporosis occurring among different patients—symptoms suggestive of some hormonal influence of the Cushing's type—were reported.

The older prepuberty female children usually do not menstruate even though the period of puberty has been reached. There have been 4 recorded cases of menstruation, 1 by Bullock and Sequiera, 1 by Walters, Wilder, and Kepler, and 1 each by Riché and Gaudier. As yet no reports have been made upon the excretion of estrogens in these cases and there is a possibility that these tumors may have elaborated steroids with such actions. Theoretically it is possible for such a tumor to occur producing female sexual maturity in a child, but none have as yet been recorded.

The older children are more apt to develop a more general hirsutism on the face and lips as well as on the body. Deepening of the voice is frequently present. Of particular interest has been the transitory rapid growth, followed by closure of the epiphyses and later relative shortness of the individual. From recent experiments it seems as if this may be the effect upon the epiphyses of excess androgens (Rapfogel, McCullagh, and McGurl).

The operative results in these female children have been surprisingly good. The first successful removal of a tumor of a normally situated gland was done in a female child by Collett in 1924. Lisser was able to collect 7 successful cases up to 1939. From the description of the cases, the successful results apparently were in those with only sex syndromes. Among the records of the unsuccessful results have been frequently recorded symptoms suggestive of other metabolic changes. Ten patients dying at operation, or within 3 days, suggest that beside surgical shock acute adrenal deficiency might have been responsible.

In adult females causing changes toward adult masculinity. In the female after puberty and before the menopause there occurs what is frequently called the adrenogenital syndrome. According to Wintersteiner this, in its broadest sense, comprises all conditions in which the abnormal changes in the sexual sphere are referable to organic or functional disturbances in the adrenal cortex. In females it consists of the appearance of male secondary sex characteristics, and the repression of female characteristics and function. Apert called it adrenal virilism. When the syndrome becomes established after puberty or later in life, hirsutism is the first change noted, followed by irregularity or cessation of the menses, changes in the body contour, and enlargement of the clitoris.

This type of virilism is not infrequent. We have examined several hundred females showing some or all of its symptoms. From thorough study of these cases we have found that the anatomical condition of adrenal gland often bears no definite relation to the type or severity of the symptoms. The glands with the syndrome may be often grossly normal, slightly or considerably hyperplastic.

Tumor is not a frequent cause of the syndrome. When tumor occurs the first symptom has been scantiness of menstruation followed by cessation. When the menses cease, the cessation has been complete. Frequently headache may occur at the time when menstruation should have occurred. Associated with the absence of menstruation has been a lack of sexual desire. Transfer of sex attraction to females was reported by Holmes followed by normal return to the opposite sex after removal of the tumor. Preceding the cessation of the menses, or coincidental with, or shortly afterwards, there is a marked increase of the

growth of hair on face, and body, all resembling the masculine distribution. Acne may occur on face or chest. The voice frequently becomes deeper and masculine in tone which has been explained as a lengthening of the vocal cords.

Changes occur in the secondary sex organs, but this change is a slower one than that seen in the menses and the hair. The younger the individual the more pronounced are the secondary sex changes. The usual sex organ changes are hypertrophy of the clitoris, deepening of the color of the labia, occasionally atrophy of the uterus and atrophy and loss of sensitivity of the ovaries. In young females the breasts may stay undeveloped, resembling a boy at puberty. In older women atrophy may occur.

These changes have been shown to be associated with the appearance of excessive amounts of androgens in the urine. The amount of androgens excreted is proportionate to the masculinity changes that have occurred. The amount may be far above that excreted by males. From one of our cases Gallagher reported 480 international units per day and the average value for normal male in his estimation was 40 international units per day. The highest recorded figure has been in the case described by Slot in which the excretion was 2200 international units per liter. The male hormone isolated from the urine in some of these tumor cases has been identified as dehydroisoandrosterone.

Among our female adrenal tumor cases with hormonal syndromes, have been 2 in which the only apparent change was that which could be produced by excess androgens.

Case 6. G.C., Chart No. 445624, Presbyterian Hospital, reported in 1936, aged 16 years, was admitted in 1935 complaining of hair upon the face and body, a deep voice, and no menstruation. At the age of 13 she menstruated for 2 periods and then had complete cessation. Her hair became thicker and darker and grew on her face, arms, legs, and body. She sang bass and was troubled with acne. She had grown practically not at all since 13 years of age, but was very active and athletic. There was marked hypertrophy of the clitoris. The blood counts, chemistry, basal metabolic rate, glucose tolerance, and visual field determinations were normal. X-ray film showed fusion of all epiphyses. The left kidney was lower than the right and intravenous pyelograms showed normal anatomical and functioning kidneys. Air insufflation roentgenograms revealed a small right adrenal and a large adrenal tumor mass above the left kidney. She excreted in her urine 8 rat units follicular hormones in 24 hours. Male hormonal excretion was estimated as 480 international units in 24 hours. The left adrenal tumor was removed through an oblique subcostal transperitoneal approach. Her recovery was uneventful and rapid. Her menses returned in 28 days and have been normal for over 5 years. Her voice gradually registered higher. She has not grown since in height but her figure has become heavier and markedly feminine. The excess hair came off her body most markedly at menstruation, but her facial "beard" has persisted, but to a less degree. Air insufflation roentgenograms of the right adrenal taken a little over 1 month after the operation showed that that adrenal had hypertrophied. Estimation of her hormonal output 6 months after operation showed that both were in normal range.

Microscopic sections of the tumor showed areas of cells in loose strands arranged in masses and sheets, resembling in some places the reticulate zone and in others the glomerular zone but in most not resembling any particular area. No mitoses were seen but there was an apparent invasion of the capsule, and there were tumor cells in the blood vessels. A few areas of necrosis were present. There were also present numerous cells with vacuoles, which apparently consisted of lipoids.

Case 7. R.R., Chart No. 571704, Presbyterian Hospital, aged 18 years, was seen in 1939 complaining of hair on face and body and lack of menstruation. She had had normal menses from the age of 12 up to 5 months before admission. She then missed 1 period, which was followed by a scanty period and there had been none since. At the same time hair appeared on her upper lip, chin, cheeks, chest and buttocks. Hair grew long upon her arms and legs and became darker. Her voice deepened. She had no pain or any other symptom. Her figure resembled a young male adult with male hair distribution. There was a hypertrophy of the clitoris and slight hypertrophy of the labia. The pelvic organs were normal except for a loss of usual ovarian sensitivity. There was no hypertension. The blood counts and the chemistry were normal. Basal metabolic rate, visual field, and glucose tolerance tests were normal. X-ray films of skull, chest, and abdomen showed no abnormality. Air insufflation roentgenograms showed an ovoid tumor of the outer portion of the left adrenal. The right adrenal appeared normal. The excretion of male hormone in her urine was approximately 190 international units in 24 hours. During the same period she excreted 33 rat units of female sex hormones. At operation an ovoid tumor of the outer portion of the left adrenal was resected from the inner or normal portion through a left oblique transperitoneal approach. She made an uneventful recovery. Her menses returned to normal 2 months after operation.

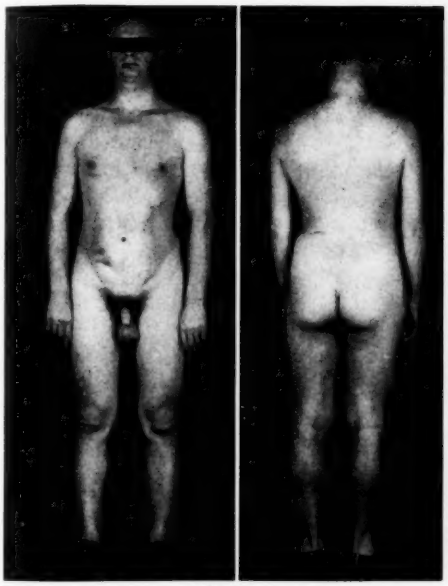

Fig. 2.

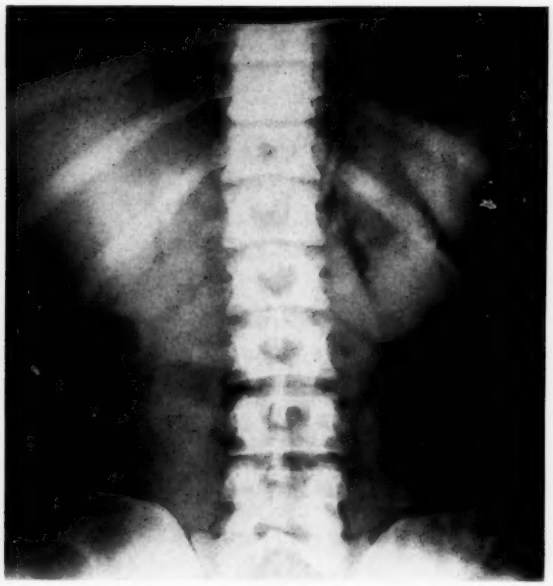

Fig. 3.

Fig. 2. Case 3. S.S., male, 36 years old, with left cortical adrenal tumor without hormonal changes.

Fig. 3. Case 3. Air insufflation x-ray film of left adrenal tumor. The ovoid shadow superimposes upon the upper pole of the left kidney and the narrow compressed band of normal adrenal is visualized, near the side of the body of the 12th thoracic vertebral body.

Microscopic sections of the tumor removed showed a small area of normal adrenal tissue. The remainder was a tumor resembling in portions the glomerular area but mostly either without definite arrangement or in spots resembling the fasiculate and reticulate zones. The cells varied in shape, the nuclei were mostly round, the cytoplasm was granular, and at times sparse. There were no mitoses seen. Vacuolated cells probably containing lipoids were frequent.

Following her operation her breasts increased and the hair became less upon her body. Her voice became higher pitched. In the 6th, 12th, and 18th weeks following operation the excretion of hormones in her urine was 6 international units male hormone and 35 rat units female hormone in 24 hours.

She progressed without change in her menstruation but the hair remained upon her chin and neck. An insufflation air x-ray film of her untouched right adrenal, taken in 1940, showed that the lower end had become rounded and wider. In March, 1941, she noticed that her menses had become scantier and that her hair growth was somewhat more vigorous. She was readmitted to the hospital and insufflation air x-ray films were taken showing that the lower end of the right adrenal had become rounded and resembled a tumor. Her excretion of androgens in the urine had again increased above normal.

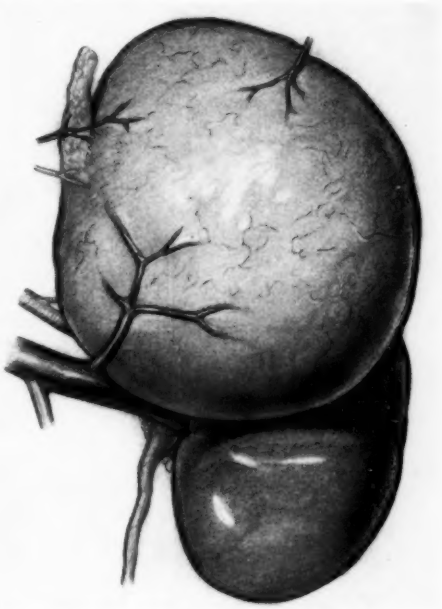

Fig. 4. Drawing representing the tumor, the adrenal, and the kidney in Case 3.

Fig. 5. Air insufflation x-ray film of bilateral adrenal hyperplasia in a female, 4 years of age, with pseudosexual precocity. There was no tumor in this case.

She was again operated upon in April, 1941, and an ovoid tumor the size of a plum was resected off the lower pole of the right adrenal through a lumbar incision. She made an uneventful recovery. Following the operation she resumed her normal menstruation with the exception that they were accompanied by premenstrual pains, the first that she had had since the cessation of menses previous to the onset of the left adrenal syndrome.

Histological section of the right adrenal resembled that of the left. There were many cells containing lipoid vacuoles.

These 2 cases presented tumors with secretion of marked excess of androgens. The androgens in both produced masculinization, less in the case with less hormones and marked in the case of excessive excretion. The diagnosis was confirmed in each by air insufflation x-ray films.

Removal of the tumors in each of these was not accompanied by acute adrenal deficiency because with only excess androgens secreted there was no reasonable expectation of function atrophy of the opposite adrenal. The uneventful recoveries support that reasoning. Following the removal of the tumors

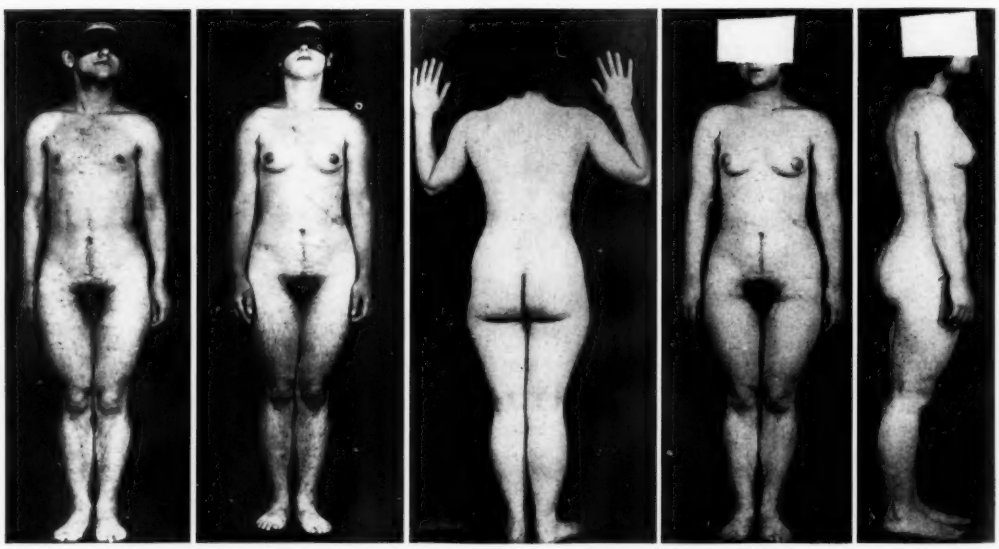

Fig. 6.

Fig. 7.

Fig. 6. Case 6. G.C., a girl of 16 with a tumor of the left adrenal with marked androgenic changes for 2 years. The left figure is before operation showing male torso and marked hirsuties. The right figure shows the change in 1 month after tumor was removed. In this picture, the figure is feminine, the breasts have hypertrophied and the hirsuties is less.

Fig. 7. Case 6. G.C., 4 years after operation. The figure is still the same height, is decidedly feminine and with markedly less hirsutism.

the excretion of excess androgens in the urine disappeared and there was a gradual diminution of the male characteristics and a restoration of the repressed female appearance and function.

Changes in a male child toward adult masculinity. The usual syndrome described with adrenal cortical tumor in a male child has been that of precocious puberty (pubertas praecox). In a very few cases tumors of the pineal gland have been responsible for sexual precocity in boys (Weinberger and Grant). Three cases have been reported as having been caused by tumors of the testis (Sacchi, Moreau, Parkes-Weber, and Rowland). A number of cases have been described in the literature without any proved cause. Among these has been a description of its familial tendency without tumor by Rush, Bilderback, Slocum, and Rogers under the term macrogenitosomia. The occurrence of the syndrome as caused by adrenal cortical tumor is uncommon. Kepler summarized its frequency as 12 times among 37 known adrenal tumors in children, a proportion of about 2 female children with pseudo-pubertas praecox to 1 male with pubertas praecox.

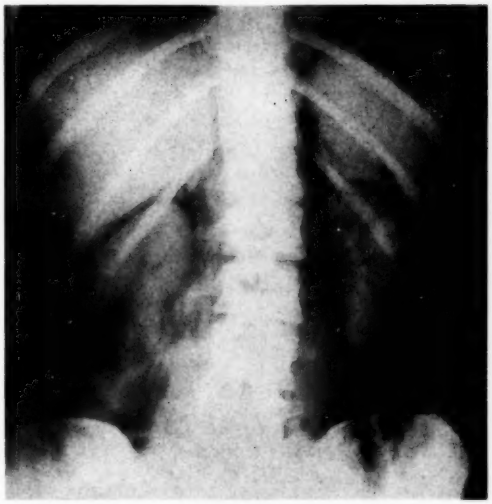

Fig. 10. Case 7. Air insufflation x-ray films showing both adrenals. The ovoid mass above the left kidney clearly shows as an adrenal tumor.

Among the earlier cases was that reported by Linser in 1903, a boy of 5 with a left adrenal tumor with metastases. The second was by Adams in 1905. Player and Lisser re-

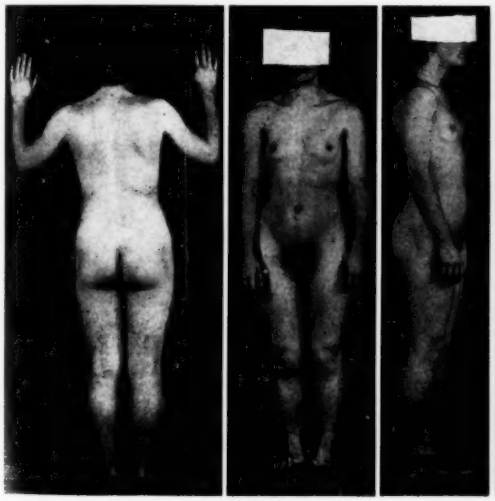

Fig. 8.

Fig. 8. Case 7. R.R., 18 years, with a tumor of the left cortical adrenal with androgenic changes for 6 months. Her figure is male, her breasts flat. She has hirsuties.

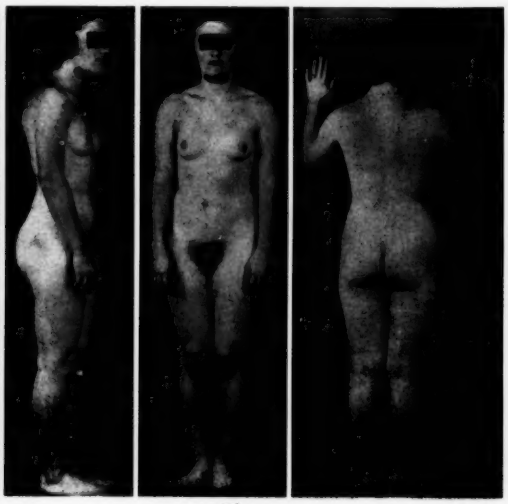

Fig. 9.

Fig. 9. Case 7. R.R., 1 year after removal of a left adrenal tumor. Her figure and breasts are feminine but some hirsutism has persisted.

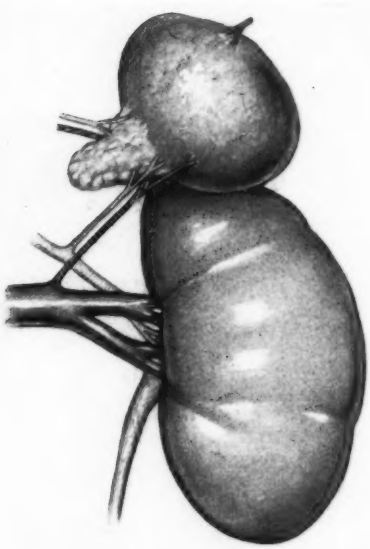

Fig. 11. Case 7. Drawing showing the ovoid adrenal tumor growing from the outer portion of the adrenal; the inner portion was normal.

ported that up to 1932 only 8 authentic cases were found in the literature and they added theirs as the 9th. They also called attention to 2 cases reported in the literature by Laborde and by Marquand, both of which had not been proved.

Cases of the syndromes must occur rarely without reporting, either because of the marked advance of the disease before recognition, so that no operative procedure was undertaken and no autopsy was possible to prove the diagnosis. Broster in an exhaustive study of the subject recorded only 1 case of a male child with prematurity. Ian Fraser has recently published the occurrence of precocious puberty in a child of 1 year. From the few cases recorded the occurrence of pubertas praecox with adrenal tumor in male children is among the rarer adrenal tumors.

We have studied 5 male children with prematurity: 5, 6, 8, 11, and 11 years of age. The 3 youngest presented masculine hair on genitals, body, beginning on the face, associated with enlargement of the penis. In these 3 the testes were not proportionately enlarged. The 3 children were much larger than normal for their age and showed advance dentition and epiphyseal development. They had no adiposity or other metabolic change. Two showed no change in sella, no evidence of pineal enlargement, no change in the thymus and nor-

Fig. 12. Case 7. Air insufflation x-ray film of her normal adrenal at the time her left adrenal tumor was operated upon.

Fig. 13. Case 7. Air insufflation x-ray film 1 year later showing the beginning of a rounded tumor growth of the lower part of the right adrenal.

mal sized adrenals by air insufflation x-ray films. One case, aged 6 years, showed a normal adrenal on the right and a large adrenal on the left by air insufflation x-ray film. This was not confirmed because no operation was permitted and the case was removed from study after operation was suggested.

Two boys, aged 11 years, showed marked hirsutism and hypertrophy of the genitals, including the testes. Their symptoms had been present, one for 8 and the other for 7 years. Their advancing maturity showed itself by fusion of all the epiphyses with apparent shortening of the extremities, and with their continued facial and muscular growth they resembled achondrodystrophic dwarfs but x-ray studies definitely disproved this dystrophy. Both had prostatic secretion and sperm. One of these boys showed no apparent change from normal in his adrenals by air insufflation x-ray films. The other had an increase in size of his right adrenal. No determination of its pathology was possible as no operative procedure was permitted. These cases resembled closely the description of familial pubertas praecox reported by Rush et al.

CASE 8. An additional case was observed by one of us (case of Dr. O. Pickhard) in a boy of 5 years in the terminal stage of the syndrome. This patient showed facial and neck obesity, as well as body obesity, genital hypertrophy, and a huge abdominal tumor.

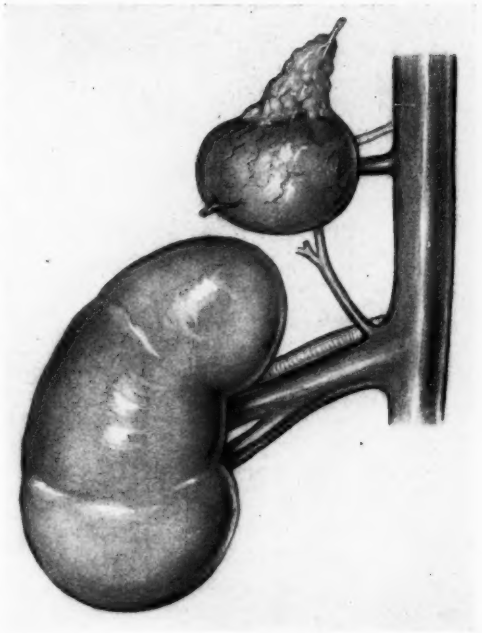

Fig. 15. Case 7. Drawing showing the rounded tumor of the lower end of the right adrenal as disclosed at operation.

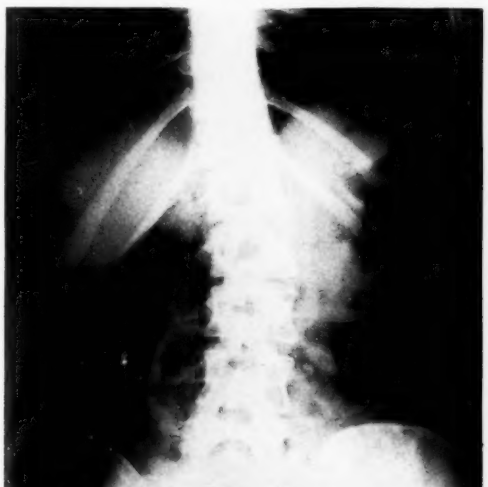

Fig. 14. Case 7. Air insufflation x-ray film 1½ years after operation, showing the increase in size of the rounded lower end of the right adrenal as compared with Figure 13.

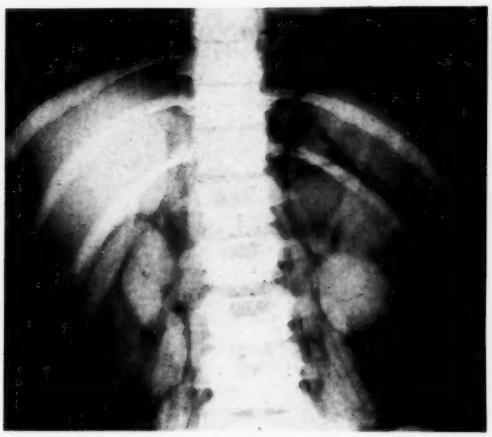

Fig. 16. Air insufflation x-ray film of a boy of 6 years with prematurity. The right adrenal was normal, the left enlarged, whether hyperplasia or tumor not ascertained.

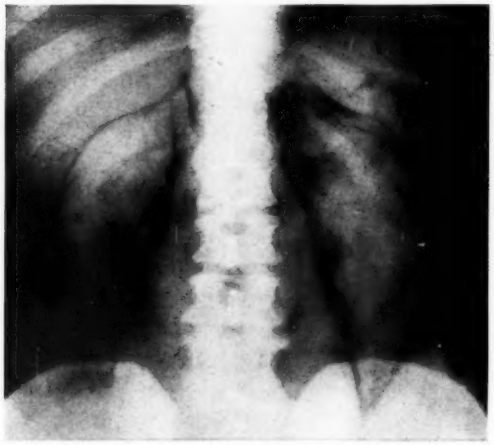

Fig. 17. Case 9. Air insufflation x-ray film in a male of 53 with some feminizing symptoms. The left adrenal is definitely enlarged and looks like a tumor on its inner side. No operation permitted.

Operative results on the few boys with the syndrome have had a very high mortality. In addition to the prematurity most obviously due to the effect of androgens, there appears very frequently symptoms suggestive of the changes seen with Cushing's syndrome and probably resulting functional atrophy of the opposing adrenal. In Fordyce and Evans' case practically no adrenal tissue was found at autopsy on the opposite side. Player and Lisser's case, the first surgical recovery in this group, showed only the androgenic effect in his masculine maturity and in the acceleration of his epiphyseal growth. He showed no evidence of acute adrenal deficiency following the removal of his tumor and made an uneventful recovery.

TUMORS WITH EXCESS ESTROGENS

Only 6 definite cases of tumors with excess estrogens producing changes in the adult male toward feminity have been reported. The first was by Bittorf in 1919, a male of 26 years noticed decrease in the size of his testes and enlargement of his breasts. He became impotent and developed a tumor in the left side of his abdomen. Cachexia and death followed, and autopsy (Matthias) showed a "malignant adrenal cortical hypernephroma." Zum Busch reported a similar case with secretion from his breasts and the cause verified by autopsy. Holl reported a patient, 15 years old who was operated upon, the diagnosis established, but the tumor impossible to remove. He reported a second patient, 44 years old, with similar symptoms in which the tumor was removed by operation and recovery. Following recovery there was a subsidence of breasts, adiposity, and varicoceles and a return of libido and sex function. Lisser published autopsy findings in a male of 33 years with breast enlargement and secretion and an adrenal cortical carcinoma. Simpson and Joll in 1938 published an exhaustive investigation into a patient, aged 34 years, who had feminization due to an adrenal carcinoma and excreted an excess of estrogenic hormone (probably estrone). The excess of hormone disappeared after the operation and returned with the recurrence of the tumor in the form of metastases. From the report of their case it is apparent that considerable proof is offered to explain the symptomatology of theirs and the previous cases.

Among the various cases referred to the Squier Clinic for adrenal determination was the following:

Case 9. H.F., Chart No. 496269, Presbyterian Hospital, aged 53 years, was admitted in 1937 with a gnawing sensation in his stomach. He noticed that for 3 years before admission his hair had become finer than previously and was increasing over his body. He gained in weight and his breasts began to increase and be noticeable. He noticed a rather marked decrease in his penis and testes and a complete loss of desire and libido. He became easily fatigued and nervous. Areas of pigmentation developed upon his hands, face, and neck. His blood pressure was low. He had a slight erythrocytosis, a normal sugar tolerance, and normal blood chemistry. X-ray studies of his head and chest showed no particular abnormality. Perirenal air insufflation x-ray films showed a large right adrenal and a marked increase in the size of his left. Hormonal studies were not made due to his departure. There was no determined cause for his feminization but from observation upon hundreds of air insufflation studies of the adrenals, he presented a shadow which showed a left adrenal many times the size of that normally seen and from its anatomical change suggested adrenal pathology.

From the few cases in the literature and especially from the one reported by Simpson and Joll, the adrenal in these cases was directly

responsible for the feminization, and the adrenal tumor cells were the source of the estrogenic hormone producing the symptoms. It was also shown by Simpson and Joll that androgens were still excreted by their patient. They attempted to show that histologically their case differed from an adrenal cortical tumor producing androgens, in one case of such with which they were familiar. Both tumors had numerous vacuolated cells, probably lipoids. They were unable to find fuchsin staining granules in the cells of the estrogenic tumor but they were present in the cells of the virilizing tumor. In the estrogenic tumor the cytoplasms of the cells were reported as diffusely fuchsinophilic. They suggested that from some studies on normal adrenals it appeared that granules were present in males in the inner layer of the cortex. In females they were not present except in patients over 50 years of age. Sudds in investigations on much larger number of adrenals, finding that granules are present in both sexes, concluded that they had little to do with sex and considerable to do with age.

Two of the reported patients with estrogenic tumors recovered from the operation when the tumor was removed and in neither was removal of the tumor followed by acute adrenal deficiency.

TUMORS WITH SYMPTOMS DUE TO EXCESS ANDROGENS AND OTHER HORMONES

From a study of the literature tumors with symptoms due to excess androgens and other hormones are not as infrequent as the others. In the large number of cases referred to us for determination of the adrenal status, this type appeared in many of the cases. A large number of the patients showed no apparent anatomical change in either adrenal. A considerable number had hypertrophy of one or both adrenals. A few had tumors as a causation. From the literature it probably is the most frequent type of tumor seen.

The syndrome was described by Cushing and he first suggested that it occurred with basophilic adenoma of the pituitary. The symptoms and clinical picture of his syndrome are characteristic of these types of adrenocortical tumors. Cushing outlined a clinical

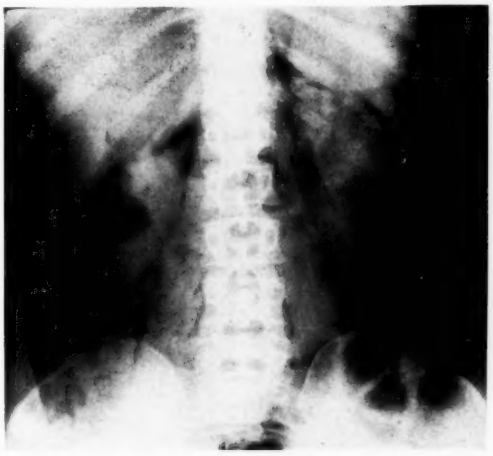

Fig. 18. Case 10. Air insufflation x-ray film in a woman of 36 years with a small right adrenal cortical tumor and a tiny left adrenal. Her symptoms were androgenic as well as of the Cushing's type.

picture consisting of a rapid, plethoric, painful obesity, affecting primarily the face, neck, and abdomen but usually sparing the limbs, thus giving rise to an obesity described as the "buffalo type." The facial changes made the eyes appear small and slit-like, resembling a pig's eye. There was acrocyanosis, with purplish linear atrophiae on the lower abdomen and the thighs. Hirsuties was marked. There was a tendency toward polycythemia and hypertension and glycosuria was of frequent occurrence, as were high blood cholesterol readings. With the syndrome was muscular weakness and porosis of the bones causing a cervicodorsal stoop and a shortening of the stature. Amenorrhea was present in the females and impotence in the males. There was a marked susceptibility to infectious processes and to physical stress. Mental changes were present, and in some, well developed psychoses occurred.

Since the description by Cushing, many reports have been issued as to the findings in these cases in which opinions have varied as to the causation. Some believe it mostly pituitary (Pardee). Others reported that it was more frequently associated with adrenal changes (Oppenheimer et al., Silver, etc.). Some similar syndromes have been reported

Fig. 19. Case 11. Air insufflation x-ray film in a woman of 40 years with a huge tumor of the right adrenal cortex. The air did not diffuse between the liver and the tumor because those fascial planes were sealed by adhesions.

as having been associated with thymic tumors. A few rare cases with obesity and hypertension as well as hirsuties have occurred with the arrhenoblastomas described by Robert Meyer.

From a study of the recorded cases with the probable causation factors as far as hormonal changes have been registered upon the patient, some of the changes could most likely have been due to the effects of excess androgens. These changes were the hirsuties, amenorrhea, and changes in the secondary sex organs as breasts and clitoris. Some of the cases exhibited these changes to a marked degree, others less. The fat deposits, the skin, the polycythemia, the hypertension, and glycosuria as well as the weakness and osteoporosis can best be explained by excess hormones present, disorganizing such metabolic processes. Bauer called attention to the fact that these in their main effects were the opposite to Addison's disease and that most of these individuals were suffering from an excess of metabolism steroids produced by the adrenal, either by itself or through stimulation of the pituitary. Considerable support to this has been offered by clinical observers and by investigators.

When tumor occurs the cases may vary from those with marked sex changes and milder Cushing type changes to those with less marked sex changes and mostly of the syndrome described by Cushing.

The following 3 cases show the variations:

Case 10. I.P., Chart No. 450269, Presbyterian Hospital, reported 1936, a married woman aged 36 years, was admitted in 1935 with loss of hair of her scalp, excess of hair over her body, and absence of menstruation for 3 years. She had become stouter and was very nervous and had attacks of weakness. There was hypertrophy of her clitoris. She had a mild erythrocytosis but her chemistry, basal metabolic rate, etc. were normal. X-ray films of skull, chest, and abdomen showed no abnormality. Cystoscopy and pyelography were normal. Air insufflation x-ray films showed an ovoid tumor of the right adrenal and a small left adrenal. She excreted 69 international units of male hormones in 24 hours. During her study she was flighty and depressed at times and emotionally unstable. Her right adrenal tumor was removed through an oblique transperitoneal incision. She developed an acute adrenal deficiency, and in spite of saline, blood, and the then available cortical extracts, she died following a convulsion 32 hours after operation. No autopsy was permitted.

The tumor on section was very cellular and not well encapsulated, and through most of the tumor were cells in sheets, cords, and nests. The cells were large with pale vesicular nuclei and indistinct nuclei. There was an occasional mitosis and tumor cells were found in the fat adjacent to the tumor. There were areas of necrosis. The cytoplasm of the cells was abundant, granular, and many were so vacuolated as to be foamy.

Case 11. L.F., Chart No. 249269, Presbyterian Hospital, reported in 1936, a female, aged 36 years, was admitted in 1929 with headaches, weakness, palpitation, excessive growth of hair, and cessation of menses for 2½ years. She was married and had two children. Her face and hands were reddened, dusky, and puffy and she had edema of shoulders and abdomen and striae of abdomen and thighs. There was marked acne of face and chest. There was an indistinct mass in the right flank, a hypertrophy of the clitoris, and insensitivity of the ovaries. She showed an erythrocytosis, normal blood chemistry, a high basal metabolic rate, a low sugar tolerance, and hypertension. She excreted 8 rat units follicular hormones in her urine in 24 hours. X-ray studies of skull and chest showed no abnormalities. The right kidney was low but no abnormality by pyelogram. Air insufflation x-ray film showed a large mass above the right kidney. The air did not diffuse between the liver and the mass. This mass, an adrenal tumor, was removed through a transperitoneal approach. It was adherent to liver and vena cava. She developed an acute adrenal deficiency in 24 hours but

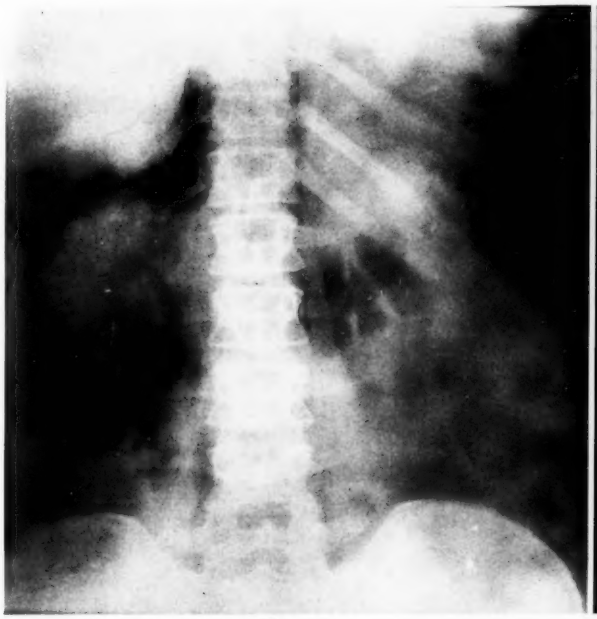

Fig. 20.

Fig. 20. Case 12. Air insufflation x-ray film in a woman of 40 years with androgenic symptoms as well as Cushing's, showing a similar irregular mass above the right kidney resembling Case 11.

Fig. 21.

Fig. 21. Photograph of Case 12, showing duskiness of hands and neck, cervicodorsal stoop, trunk and face obesity, and thinness of hands and legs, abdominal striae, and mild hirsuties.

recovered with saline and blood transfusions. Her menses returned after 2 months and her hair diminished in amount. She returned to her marital status with return of libido. Six months later she developed headaches and her menses became scanty at first and then ceased. X-ray films showed lung metastases. The hair growth, duskiness of hands and feet, and edemas progressed. When she died no autopsy was permitted.

The tumor on section showed that the morphology was almost identical in all parts. There was no resemblance to a normal adrenal. There were many mitoses and cellular invasion of the stroma. Many cells were vacuolated and foamy cells were frequent.

CASE 12. E.G., Chart No. 304917, Presbyterian Hospital, a female, aged 40 years, was admitted in 1939 with complaints of hair on body, increased fatty deposits, and absence of menses. For several years her entire appearance had changed with gain of fat on face, neck, chest, and abdomen with loss of size of arms and legs. Her face, chest, and hands were reddened. She had marked striae on the abdomen and thighs. With this change her menses had ceased. She had dyspnea and edema of her feet. Her clitoris and labia were enlarged. She had erythrocytosis, a normal blood chemistry, a low basal metabolic rate, and low sugar tolerance and a high blood cholesterol reading. There was moderate hypertension and a rather moderate cervical dorsal stoop. X-ray films of her skull, bones, and chest showed no abnormalities. Air insufflation of the perirenal space showed an apparent large mass above a low right kidney resembling that in Case 11. There was no follicular hormone in her urine and only a small amount of follicle stimulating hormone was present. Male hormonal excretion determination was not done. She was not operated upon but condition became worse and she returned to Poland. Since then she has been untraced.

These 3 cases appear to be illustrative of the variations produced by different effects. The first had well marked effects of excess androgens and moderate other metabolic disturbances and the last with slight change in sexual characteristics and well marked metabolic disturbances. These cases differed markedly from the 2 younger women in the emotional balance. In fact it seems as if the Cushing type tumor appears more frequently in the older group of women. The cases with only androgen syndromes were stolid, not nervous.

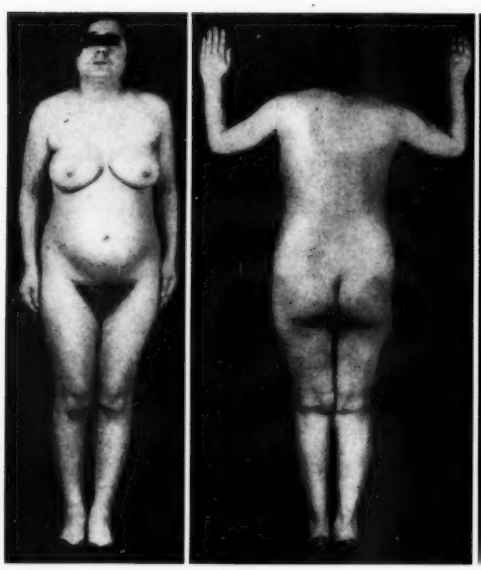

Fig. 22.

Fig. 22. Case 13. Photograph of female aged 27 years with syndrome of Cushing's type without androgenic changes. She had a tumor of her left adrenal cortex.

Fig. 23.

Fig. 23. Case 13. Air insufflation x-ray film in which the air diffusing poorly shows a normal sized right adrenal and a tumor of the left adrenal above her left kidney.

took all examinations without any disturbance. Those with the other changes were nervous, apprehensive, and difficult to handle. The demonstration of the tumor by air injection became less clearly defined as the patients developed fatty deposits and edemas. In 1 case, the second, the air did not diffuse between the tumor and the liver or around the mesial aspect. Operation disclosed that tumor adhesion had sealed the fascial planes in this area. The last patient, not operated upon, presented a similar air infiltration x-ray film. The first case was proved to have an excess of male sex hormones excreted in her urine. The second case most probably had a large excess but at that period there was no satisfactory process available for its estimation. She, however, excreted normal amounts of female hormones. The 2 patients operated upon developed postoperative symptoms of acute adrenal deficiency. One patient died in spite of therapy now known as inadequate. The other patient recovered from her acute deficiency. We thought at first the recovery was brought about by our therapeutic endeavors but later experience leads us to think that the hormonal production of her unrecognized metastases may have played the major part in her recovery.

TUMORS WITH CHANGES DUE TO EXCESS OTHER STEROIDS RELATED TO METABOLISM

Case 13. L.G., Chart No. 509497, Presbyterian Hospital, a female, aged 27 years, was admitted in 1937 with a marked depression, melancholia and with a suspected endocrine pathology. Up to 2 years before admission she was a normal married woman, working as a journalist and editor. She then underwent a marked change in personality, lost all interest in her surroundings, contacts, and body needs. At the same time her menses ceased and a fine silky growth of hair appeared upon her face, body, and extremities. There was no resemblance of male distribution. There was swelling and duskiness of face and hands, swelling of neck, shoulders, and abdomen with striae on her abdomen. She had a cervical thoracic stoop. She was apathetic and sat long periods without speaking or moving and walked falteringly. She stated that she was mentally unbalanced. Her clitoris was small as were her pelvic organs. She had an erythrocytosis, a normal blood chemistry with high cholesterol readings. A low sugar tolerance and a normal basal metabolic rate. There was mod-

crate hypertension. The x-ray films revealed no abnormalities of head, chest, or bones. Perirenal air insufflation x-ray films were difficult to read because of poor diffusion of the air. However, by serial readings a normal appearing right adrenal was identified and a triangular shaped tumor on the left was noted. There were no demonstrable male or female sex hormones in her urine by our ordinary comparative examinations. At operation a left adrenal tumor was removed through a subcostal transperitoneal incision. She reacted excellently from the anesthesia and on recovery from unconsciousness was talkative, and chatty, greeted her relatives the first time since the onset of her syndrome and stated that she no longer felt unbalanced. Her relatives declared she acted like her former self. She was given large amounts of saline and commercial cortical extract then available. In 20 hours she developed acute adrenal deficiency, was benefited slightly by transfusion and cortical extract but died after a convulsion in 23 hours after the operation.

A complete autopsy showed Cushing's syndrome (clinical) hirsutism (silky not masculine) adiposity, adenoma of adrenal cortex, left, (surgically removed), atrophy of adrenal cortex, right; encephalomalacia, frontal, right; fatty liver, normal ovaries, thyroid and pineal. In the pituitary, all basophiles showed marked hyaline changes in their cytoplasm. Partial to complete disappearance of the granules, vacuolization and disfiguration of the nuclei (Crooke syndrome).

The left adrenal tumor showed a small group of cells alternating with much larger cells which had a foam cell appearance. The true adrenal cortical zones were not seen. The group of cells seen were large, polygonal, possessing oval nuclei with distinct nucleoli and were at times vacuolated. The foam cells appeared multinuclear with rather small nuclei and pale framework within the cytoplasm. A tendency to giant formation was rarely seen.

This patient had the symptoms described as Cushing's syndrome with cessation of menstruation, the only real change of sexual character. No male or female urinary hormones were identified by the usual examination. The complete autopsy did not reveal any change in the pituitary except that described by Crooke. It is to be deduced that the adrenal cortical tumor produced the changes manifested by her symptoms for the 2 years prior to her operation. The death was due to acute adrenal cortical deficiency. The remaining adrenal was apparently atrophic and inactive. In retrospect the tumor must have produced sterols in abundance as was evidenced by the histological sections in which most of the cells were foamy with lipoids. These sterols were neither of androgenic nor estrogenic influence as was shown by her symptoms and the failure to identify either in her urine. From her symptoms and acute death following the removal of the tumor they apparently had to do with the life maintenance properties of the adrenal.

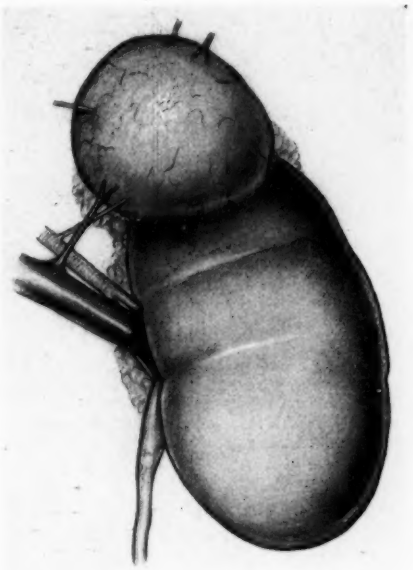

Fig. 24. Case 13. A drawing of the tumor and kidney at the time of operation.

DIAGNOSIS WITH AIR INSUFFLATION X-RAY FILMS

For the purpose of ascertaining the anatomical change in the adrenal gland we have used the x-ray studies of air insufflation into the perirenal fascial spaces. We have previously reported upon this technique, as have Roome, Mencher, and others. Normal adrenals are usually well visualized if sufficient air is introduced in the proper plane. The right adrenal more frequently shows as a long thin wedge between the liver and the psoas and the left as a less dense wider wedge or crescent above the left kidney. When tumor is present it is more clearly shown in thin people. The tumors are round when small, ovoid when larger, and may be lobulated when very large.

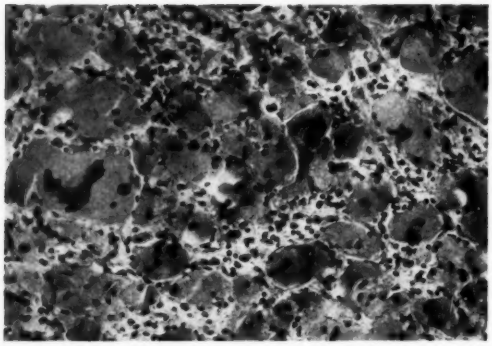

Fig. 25. Section removed in Case 3, a male without hormonal symptoms. The cells in places are gigantic with large amounts of cytoplasm and huge nuclei. Lipoid vacuoles are rare. All male cases without hormonal symptoms had similar histology. ×160.

All of the tumors so diagnosed by us were confirmed by operation. In a number of cases in which no tumor was shown on the air insufflation x-ray films, but with some hypertrophy apparently present, operative procedures have always demonstrated that the adrenal was exactly as outlined. It was especially valuable when tumor was present and small and unrecognizable by any other method, except operation. It will also show the presence of the opposite adrenal if one is the seat of a tumor. In children and in thin adults the air diffusion is easy and gives clear shadows. In obese and especially in those with Cushing's syndrome, the air diffuses poorly because of the fatty edema in the perirenal tissues. In these patients a series of films may outline parts of the tumor so that a composite film may be made. For the purpose of demonstrating adrenal anatomy, in our hands the use of air insufflation has been without complications and without fatalities. If used often it can lead to an increase in the fibrous tissue in the perirenal fat and by some this has been considered to be a hindrance during operation. Compared with the diagnostic aid obtained by its use in our hands, the increased fibrosis of the perirenal fascia was of no consequence.

The autographic x-ray film by the method of Reynaldo dos Santos has been used by some but the dangers of thorotrast have been since shown to make this media hazardous.

HORMONES

Androgens. The earlier work of the estimation of the androgenic hormones was by the capon comb growth. The method is better standardized but difficult and expensive. The colorimetric method when used, as by Callow, with proper caution as to procedure and interpretation, is simpler and less expensive and time may prove its value. There is definite agreement that virilism and adrenal cortical tumors are associated with high levels of androgen excretion and this high androgen excretion declines to lower levels after operation.

The determination of the particular hormone or hormones producing androgenic effect is a difficult procedure, requiring high output values in the urine and large amounts for assay. The hormone of the adrenal that has been isolated in this manner has been shown to be dehydroisoandrosterone, a beta kesteroid and is different from the hormone of the testis, testosterone, an alpha kesteroid. Under certain conditions the beta kesteroids are greatly increased in quantity, as in patients with hyperplasia, adenoma, and carcinoma of the adrenal cortex, and may be of value in diagnosing Cushing's syndrome due to pituitary basophilism from that due to adrenal cortical change.

In the excretion of androgens there appears to be a rather definite relation to the amount of male virilism and with the amount of androgens in the urine. The more marked the symptoms, the higher the assay.

Another kesteroid with androgenic action has been isolated from the urine, particularly that by Butler and Marrian (pregnane). This apparently was associated only with that adrenal tumor. The identification of this particular kesteroid required large amounts of urine and with mechanics and talent not available in many laboratories. Its identification was not useful for purposes of preoperative diagnosis.

There is a need of a simple and fairly reliable estimation of all the androgens excreted so that the results may be quickly available to be applied in a survey of the symptoms of each case. It is needed because the symptoms of androgenic excess are more frequent than any other.

Estrogens. Frank early called attention to the excretion of large amounts of estrogens in the urine of patients with the adrenogenital syndrome and with virilism. In our former article we called attention to the large or normal amounts so excreted. Slot and Kepler each reported cases in which there was no excess. In the series of Levy, Simpson, de Fremery, and MacBeth, a slight excess of estrogenic hormone occasionally occurred. In our present reported cases we have shown that in young girls with virilism due to a tumor a high amount of estrogens was excreted before the tumor was removed and continued unchanged after removal of the tumor and the virilism had recessed.

Of particular necessity is the estimation of the estrogens in those rare cases of males with femininity due to adrenal cortical tumor. Here, Simpson and Joll have shown that excess estrogens were evidently present before the tumor was removed, disappeared after the tumor was removed, and recurred with reappearance of the tumor. The estrogen excreted was considered to be estrone.

The identification of other kesteroids associated with adrenal cortical tumors is as yet in an unknown state. An increase in substance which maintains life was demonstrated in the blood stream of a patient with hyperfunction of the adrenal cortex (Cushing's syndrome). The identification of like-maintaining substances in the urine in normal persons and their increase under stress has been reported by Weil and Browne. There are as yet no reports upon cases of adrenal syndromes in which these other types of steroids have been identified in the urine, or whether their amount can vary according to the adrenal symptoms.

OPERATIVE PROCEDURES

Three different routes of approach have been used for removal of the adrenals (1) extraperitoneally, through the lumbar region, (2) transthoracic route, and (3) transperitoneal route.

The lumbar route with extraperitoneal approach has been used extensively in adrenal operations by Crile. It has been used for removal of tumors by many operators. Walters, with as extensive experience as any, has used this route and has done bilateral exposures to determine first the diseased side and second to observe whether there was an opposing adrenal. Young devised an ingenious retractor fashioned after the rib-spreader retractor for chest operative procedures, and used the retractor for simultaneous bilateral exposure. The lumbar route has been used by us in adrenal operations upon the nontumor cases. It was used in 3 tumor cases: (1) a small pleochromocytoma of the adrenal, (2) a small tumor of the lower pole (Case 7), and (3) one of the larger nonhormonal tumors occurring in a male. This latter was difficult to deliver, was attached to the anterior capsule of the kidney, and the tumor ruptured through the capsule when attempts were made to visualize the tumor vessels before clamping and ligature. It was necessary to remove the kidney with the tumor.

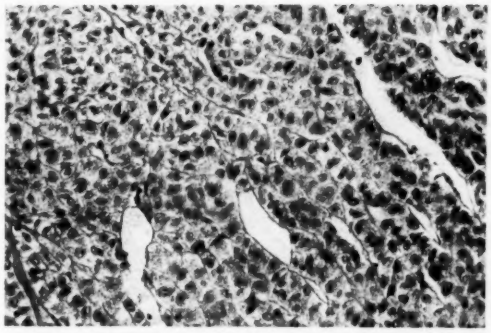

Fig. 26. Section removed in Case 5, a female without hormonal symptoms. The tumor was of an aberrant adrenal. Sheets of cells of somewhat uniform size arranged in places resembling the different zones of the adrenal. Lipoid vacuoles are rare. The adrenal tumor from the other female without hormonal symptoms had similar histology. ×160.

The transthoracic approach was used by Broster in cases of nontumor adrenogenital syndromes. This, he claimed was the easiest approach in view of the fact that the adrenal vessels allowed a slight range of upward movement. It has, however, the disadvantage of creating an artificial pneumothorax. It also was necessary to do a preliminary laparotomy for exploration of the adrenals by palpation, and then after recovery to perform the main operation by the transthoracic approach.

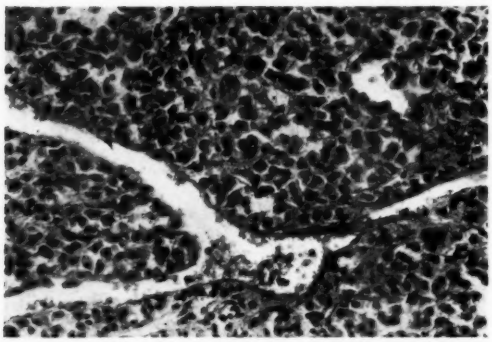

Fig. 27. Section of tumor removed in Case 6, a female with only marked androgenic symptoms. The cells stain deeply, are large in places but not like the nonhormonal male. The cytoplasm contains abundant granules and also many lipoid vacuoles and some foam cells. ×160.

We have felt that with both the lumbar and transthoracic route, the operator is too handicapped by the inadequacy of the incision and the impossibility of ligation of the vessels before the tumor is manipulated. It also is impossible to be familiar with the location of the other viscera and vessels from within the limited area above the renal pole. We think that either will give an adequate exposure for small normal or slightly enlarged adrenals. We have had no experience in the bilateral incisions of Young in adults or in cases with tumor. It is satisfactory in children with small hypertrophy of the adrenals and may be with tumor.

The transperitoneal approach that we recommended in our former report has been to us most satisfactory for an adequate exposure and to offer the greatest freedom in proper handling of a tumor, especially if it is large. The direction of growth of a tumor of the adrenal is downwards and anterior, both in the direction of the incision. The location of other viscera and of the vessels is easier and the reparation of the posterior peritoneum is possible quickly and well. There have been no weaknesses in the abdominal wall subsequent to the operation.

POSTOPERATIVE ACUTE ADRENAL DEFICIENCY

Many cases have been reported with what has been described as shock occurring immediately or shortly following the removal of an adrenal tumor. Cecil stated that 39 per cent died of this shock and that 66 per cent had severe shock from which 27 per cent of all patients operated upon recovered. The other 33 per cent apparently had no shock.

It is now accepted by most clinicians and investigators that the characteristic collapse is that of acute adrenal cortical deficiency. We have seen this collapse in the removal of a renal carcinoma which, invading the adrenal, necessitated the adrenal's removal with the perinephritic fat and the tumorous kidney. The collapse terminated fatally and autopsy disclosed that the only metastases from the renal tumor were in the opposite adrenal which had been destroyed. From a perusal of the literature and from our own experience it does not occur in the nonhormonal adrenal cortical tumor cases, or in the pure sex hormonal type cases but occurs in those which show the effects of excess hormonal action upon many metabolic factors, the electrolytes, the water and salt balance, the capillary permeability, in fact the symptoms seen in the Cushing's type, whether in children or in adults. It has been advanced on reasonable grounds that in these cases the changes can only be produced by excess hormones. It has been shown experimentally that excess life maintenance substance can cause atrophy of the adrenals. Clinically in those cases ending fatally it has been shown that contra-adrenal atrophy is present with the Cushing type tumors. It has been our experience to have a

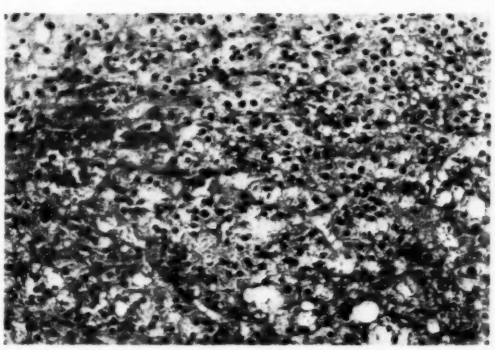

Fig. 28. Section of tumor removed in Case 7, a female with only androgenic symptoms. The cells are fairly uniform, stain deeply, have numerous fine granules, and many lipoid vacuoles and some foam cells. ×160.

patient of this type recover from the adrenal collapse without administration of a potent adrenal extract but later recognition of secreting metastases elsewhere offered the explanation. Broad and Broad reported such a case in which they first attributed the recovery to frequent administrations of adrenaline.

Walters and Kepler stated that the most important factor in surgical therapy of adrenal cortical tumors is the anticipation, prevention, and control of postoperative cortical deficiency. In this we concur but call attention to the mechanism as mostly only occurring in those of Cushing's syndrome, because with the androgenic type tumor there is no functional atrophy of the opposing adrenal.

The method is that used in the crisis of Addison's disease, having on hand and administering preoperatively and postoperatively potent adrenal hormone. A potent extract of the cortex may be used as furnished by Kendall to Walters and Kepler, or desocycorticosterone in adequate doses may be used. In addition to the hormone there is administered by oral or parenteral administration adequate amounts of sodium chloride and sodium citrate. Since the marked cases of Cushing's syndrome have an erythrocytemia, but apparently a marked diminished blood volume, an immediate postoperative transfusion is necessary. It is considered possible that a diet low in potassium might be of value for sometime preceding the operation.

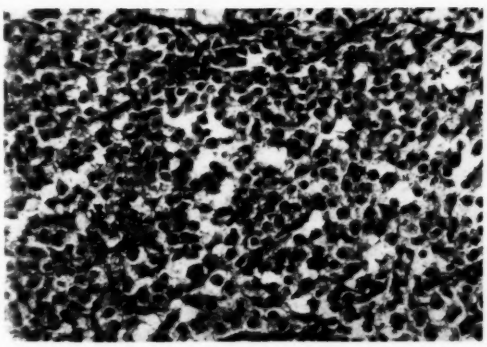

Fig. 29. Section of tumor removed in Case 11, a woman with androgenic and Cushing's symptoms. The cells are uniformly of carcinoma, some granules in the cytoplasm, and many lipoid vacuoles and foam cells are present. ×160.

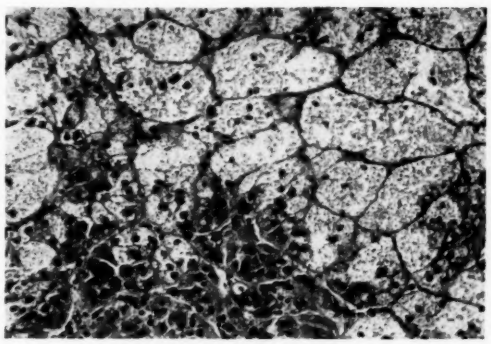

Fig. 30. Section of tumor removed in Case 13, a woman with only Cushing's symptoms and no androgenic changes. The entire tumor was composed of huge cells filled with lipoid vacuoles, like foam cells. Only in a few places were cells containing granular cytoplasm as is shown in this field. ×160.

In 1937 Ingle and Kendall reported that they were able to prevent the atrophy of the adrenals experimentally when large doses of active adrenal cortical substances were given, by the use of an anterior pituitary extract which had high adrenotrophic activity. To date there has been no report as to its effects given preoperatively upon the Cushing syndrome cases, to produce reactivity of the opposing functionless adrenal cells.

Walters and Kepler believe that they have been able to tide the patient over the crisis by replacement therapy and that the remaining adrenal tissue will regain its capacity to produce a sufficient amount of hormones to meet the needs of the body. Since the potent steroid has been available we have not had a marked Cushing's syndrome type tumor, and from our experience, those cases with androgenic changes do not need replacement therapy if an opposing adrenal can be demonstrated by air insufflation x-ray film.

PATHOLOGY

The tumors were either adenoma or carcinoma. The adenomas were soft, encapsulated tumors and histologically did not show any invasive characteristics. The cells were typical of the adrenal cortex of no particular zone and showed lipoid vacuoles which compared roughly in number with the degree of hormonal changes.

The carcinomas varied. In the 2 nonhormonal tumors in male adults the cells were frequently of giant size with giant nuclei. They resembled various parts of the adrenal. Lipoid vacuoles were rare. Sections of the specimens obtained from the females without hormonal syndromes again resembled each other. They differed from similar males in the relative rarity of the giant cells and nuclei and the variability of their appearance. At times sheets of cells resembled the glomerular zone, other places the fasiculate, and again the reticulate. In other places they were undifferentiated. They resembled sections of renal hypernephromas. In the cells lipoid vacuoles were infrequent.

Sections of the carcinomas associated with hormonal changes varied. One showed invasion of the capsule and cells in the blood vessels. The cells were in sheets resembling some parts of the adrenal cortex, more frequently the glomerular and reticulate layer. Numerous vacuoles were present. The other had cells mostly undifferentiated with many mitoses and numerous vacuoles present. The number of cell vacuoles again roughly appeared to vary with the amount of hormonal changes.

The more the syndrome approached the Cushing type, the more marked was the amount of vacuoles which were present. In the last case with only the syndrome of the Cushing type present, the number of vacuoles present was so great that most of the tumor was composed of foam cells.

In review of our attempts to correlate the finding of fuchsinophile granules with the symptoms of the disease has still left us unable to decide whether their presence has or has not any particular association with the various types of cases.

Fuchsinophile staining of the cytoplasm was present in all the tumors, in some diffusely, and in others in granules. It apparently was more pronounced in cases with hormonal syndromes.

SUMMARY

1. Adrenal cortical tumors may occur without hormonal syndromes or with hormonal syndromes.

2. The hormonal syndromes may be due to an excess of androgens or estrogens or other as yet unidentified hormones.

3. The syndromes are determined by the type and amount of hormone or hormones produced and by the sex and age of the patient.

4. The status of the adrenals may be adequately shown by air insufflation x-ray films.

5. Removal of adrenal tumors by the transperitoneal route is surgically best.

6. Acute adrenal deficiency occurs only, or mostly, in those with symptoms described as Cushing's syndrome.

7. The therapy of this is similar to that which is used in the acute deficiency crisis in Addison's disease.

8. Histologically the tumors that produce the hormonal syndromes have cytoplastic lipoid vacuoles in amounts comparable to the symptoms.

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FUNCTIONAL DISTURBANCES OF THE CHOLEDOCHUS AND HEPATIC BILE DUCTS

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IN 1917, surgeons believed that spasm, or increased tonicity, of the sphincter of Oddi, was the factor which, by mechanical action, caused biliary pain and jaundice. Shortly afterward, results of experimental research were reported which showed that cholecystectomy is frequently followed by incontinence of the sphincter of Oddi which in turn is followed by muscular hypertrophy of the sphincter, as reported by Rost. In 1925, Del Valle reported his observations on obvious stricture of the papilla of Vater seen during operation performed on cholecystectomized patients suffering from pain crises.

Further reports of experiments, as well as of findings during operations and of postoperative observations, directed the attention of surgeons to the sphincter of Oddi. In 1929, Westphal, Gleichmann, and Mann (34) were able to establish that, from a functional point of view, the antral upper part of the sphincter of Oddi is vagotonic whereas the lower part is sympathicotonic, as shown by faradic irritation in association with pharmacodynamic substances.

About the same time that functional disturbances in animals were reported, I observed, by means of operative cholangiography, spasms of the sphincter of Oddi in patients whose biliary tract had been operated upon.

In 1930, Nanu, Muscel, and Pavel reported cases of jaundice due to reflex spasm of the sphincter of Oddi which was classified as functional jaundice. Other cases were reported by Pavel and Jonckheere. More recently, several surgeons and research workers, including Walters and Doubilet and Colp (10), observed by means of manometry in addition to postoperative cholangiography, the presence of spasm after the administration of certain substances.

In 1940, I presented before the National Academy of Medicine of Buenos Aires a series of clinical observations and roentgenograms made during the operation which indicated that the existence of abnormal spasm of the hepatic duct was capable of producing biliary stagnation (21).

Method used. I studied the functions of the biliary tree by means of operative cholangiography. The procedure (19) consisted in the majority of cases in injecting through the cystic duct from 3 to 5 cubic centimeters of iodized poppyseed oil at the rate of 1 cubic centimeter a minute. A slow injection is important in order to prevent a sudden distention of the biliary tree. By this method the operation is performed under the best physiological conditions; the registered phenomena can be correctly interpreted and, at the same time, the pathological conditions can be clearly differentiated from the normal. Up to the present, this study includes 800 cases of biliary lithiasis which have been systematically observed by means of operative cholangiography.

The Sphincter of Oddi

The majority of surgeons believe that a more or less prolonged spasm of the sphincter of Oddi is the only cause of biliary stagnation. They believe that the free flow of bile is obstructed by the increased tonicity of the sphincter, the intensity and rhythm of which are controlled by several factors, in particular by diseases of the gall bladder and concretions.

The Chinese aphorism "the sum of the parts is not the total" can be applied to the field of medicine. The "functional factor" which, according to Bergmann, is the *primum movens* in

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the development of anatomic lesions escapes detection and cannot be identified by the senses.

Though one does not deny that purely functional phenomena are the predominant pathogenic factors, it is doubtful that they are the only ones, and it becomes less doubtful when one observes cases of evident permanent obstruction to the flow of bile which has lasted for several years and has been controlled only by means of an operation for drainage of bile.

Nowadays, in accordance with the modern trend of surgery based on clinical observations at each and every operation one can state by physiological standards that in the presence of any abnormal condition the living body has an anatomic substratum which exists only during life but which either disappears when death takes place or is transformed by death.

Hypertrophy of the sphincter of Oddi. The occurrence of hypertrophy of the sphincter of Oddi after cholecystectomy has been established beyond doubt by experimental research (Rost). Therefore, it is logical to assume that the same thing occurs in man. It is also logical to believe that hypertrophy is one of the factors producing a resistant papilla. The same phenomenon is frequently found in the cardia and in the rectum, in which the obstructive agent is the sphincter with its marked hypertrophy.

It is important to understand that a permanent, real anatomic factor is always added to spasm. The increased amount of contractile tissues about the sphincter, which conflicts with the anatomic and functional conditions of the common bile duct under control of the sphincter, favors the production of stagnation. Similar physiopathological facts are necessarily present in some cases, even in noncholecystectomized patients, because lithiasis in itself creates conditions similar to those which follow cholecystectomy. Moreover, lithiasis is equivalent to cholecystectomy in man. The local edema, hyperemia of the tissues and local congestion, in addition to hypertrophy of the sphincter, will complete the transient sphincteral obstruction or else they will prevent complete closure of the sphincter in the intervals of muscular relaxation. Infection may be a helpful, although not an indispensable, factor.

It is possible that in the 8 cases reported by Strauss the pathogenic mechanism corresponded to the aforementioned physiopathological facts. Strauss' patients complained of pain crises simulating hepatocolic pain without jaundice. At operation it was found that the gall bladder was inflamed but without stones; pericholecystitis was present and the hepatic and common bile ducts were dilated. Cholecystectomy was performed, but shortly afterward the patients suffered attacks similar to those which they had had before operation. A second operation was performed. It was found difficult to insert even a fine catheter through the lumen of the ampulla of Vater which was of increased consistency and the seat of infiltration. The patients were subjected to dilatation of the lumen of the ampulla of Vater; 4 were operated on a third time for recurrence of attacks. This time, choledochoduodenostomy was successful. In some of the patients the ampulla of Vater was the size of a nipple, was red, inflamed, and congested.

Anatomic obstruction. The more attention one gives to the anatomic obstruction of the sphincter of Oddi the more significant are the clinical observations. A series of cases presenting permanent obstruction at the sphincter of Oddi have been reported during the last few years, by Haberer, Sturm, Melchior, Floercken, and Colp and Doubilet (6). The existence of the anatomic substratum of stenosis of the papilla of Vater in the presence of gall-bladder disease either with or without calculi or concretions is frequent, whereas it is rarely observed at necropsy—a factor which depends on the many changes which take place during life. Physiological conditions may change at any time; a stricture of the duodenal papilla may disappear with the consequent restoration of normal tonus in the sphincter of Oddi as well as the re-establishment of the normal morphology of the biliary tree.

Physiological investigations are being carried on with due consideration of the fact that the elimination of bile through the hepatic and

common bile ducts is the explanation of the harmoniously co-ordinated functions in which peristalsis of the common bile duct, contraction of the hepatic duct, and the tonus of the sphincter of Oddi are equally important. From pathogenic and physiological angles, a papilla of Vater of normal patency in the presence of hypertrophy of the common bile duct constitutes a more or less evident obstacle to the papilla. Dilatation of the biliary tract indicates a functional disturbance even in the absence of any anatomic lesion. A spastic hypertonic papilla in a choledochus with normal tonus is also an obstacle against which the duct reacts with detrimental effect to its energy and muscular ability, thus producing dilatation of its lumen and elongation and sinuosity of the duct.

The study of tranverse sections of the distal choledochal segment including the sphincter of Oddi revealed, in 50 per cent of the cases of lithiasis, evident muscular hyperplasia, especially annular hyperplasia, and a moderate hyperplasia of the longitudinal and oblique muscular fibers.

Muscular hyperplasia was so great in these cases that, after further evolution, it caused the limiting zone between the muscular rings of the sphincter to disappear. Increase of the connective tissue was also observed in some cases, especially in those in which muscular hyperplasia did not occur. Increase of both the muscular and connective tissues occurred in some cases (Westphal, 33). These anatomic changes may take place in the choledochal segments of the sphincter of Oddi, even though the common bile duct does not contain stones.

Choledochitis and anatomic obstruction of the papilla of Vater. In 1908, surgeons of the French school, especially Gosset, discussed before the Congress of Surgery in Paris the rôle of stenotic and nonstenotic inflammation of the common bile duct without stones in the production of biliary stagnation and in the development of jaundice. Later, Charrier and Thalheimer, also surgeons of the French school, reported their observations in 27 cases of choledochitis without concretions and described the lesions which were observed in the common bile duct, the hepatic duct, the gall bladder, and the pancreas. A group of cases of choledochitis, which is secondary to cholecystitis and biliary stagnation and which follows the evolution of these conditions, is clearly differentiable in the 27 cases. The appearance of the common bile duct in some cases of this group resembles a pipe (the so called *tuyau de pipe* of French surgeons). The lumen of the duct becomes narrower with each recurrence of the inflammation until finally it is so small that even a fine probe cannot pass through. In such cases, the phenomena of biliary stagnation are aggravated by the spasm of the sphincter of Oddi. Choledochitis is an added factor of irritation (Brocq). Cases of either partial or diffuse inflammation of the common bile duct constitute a group of surgical cases of choledochitis in which interstitial sclerosis involves not only the walls of the duct but those of the ampulla of Vater as well (Chabrol and Klotz).

Argentinean surgeons, especially Del Valle, called attention to a group of cholecystectomized patients who had been operated on for the so called choledochal syndrome, namely hepatocolic pain; Oddi's sphincter was stenotic (retractile choledocho-odditis). The process of inflammation was verified by microscopic studies. I have in my files the record of a case of choledochitis with stricture of the papilla of Vater. A brief résumé of the record follows:

"Series 1. Case 24. A woman, aged 40 years, suffered from repeated attacks of hepatic pain and jaundice which were over as quickly as they appeared. An enlarged gall bladder (the size of a duck's egg), 15 centimeters in length, without stones and with thick walls, was surgically removed. The cystic duct was in free communication with the common bile duct, which was like a rigid tube, the size of the little finger. Its walls were 2 millimeters thick. A stricture of the ampulla of Vater and the absence of calculi were disclosed by means of operative cholangiography. Papillary fibrous stricture was found during duodenostomy. The ampulla of Vater was incised. The patient recovered."

Nomenclature. The names applied to the alterations in the sphincteral segment of the common bile duct vary widely because of the lack of consistency in the understanding of their etiology and pathogenesis. They include "spastic cholepathy" (Schmieden and

Niessen, 27), "dyssynergia of the common bile duct" (Best and Hicken), "biliary dyskinesia" (Ivy), "papillitis," "sphincteritis" (Walters), "resistance of Vater's papilla," "scleroretractile choledocho-odditis" (Del Valle).

Classification. Any extreme classification will be either insufficient or exaggerated. I believe that the term "odditis"[1] for all the phenomena of obstruction will properly cover the field. Odditis is then divided into dystonia and stenotic odditis.

Dystonia is evidently exhibited as a functional disorder—there is incomplete closure of the sphincter due to spasm in the distal sympathicotropic part of the sphincter only. This functional disturbance causes a reflux toward the duct of Wirsung. The phenomenon must occur in a larger number of cases than is shown by operative cholangiography. The two ducts do not open into the ampulla of Vater in all cases, and also it may not be possible to detect the phenomenon in the operative cholangiogram (see Fig. 3). Dystonia may be compared with the type of dysthyroidism of the dualists; whereas early stenotic odditis may be compared to hyperthyroidism. The former is due to a dissociated function, whereas the latter is due to an increased one. Therefore, the name dystonia is proper for that functional disorder.

Stenotic odditis is a term applied to any type of resistance of the ampulla of Vater without specifying the causes of the more or less permanent obstruction at the sphincteral segment. In some cases the resistance is due to true total hypertonicity of the sphincter of Oddi. Sclerotic retraction occurs only in rare cases.

Now then, operative cholangiography deals with the problems of the various types of dystonia and stenotic odditis with an essentially physiological criterion. Moreover it fulfills all the requirements necessary to reduce the causes of error to a minimum: The injection of the opaque substance is made slowly and in very small amounts; thus distention of the bile ducts and the entrance of foreign matter in the hepatocholedochal system are prevented and the anatomic integrity of the ducts is well preserved. The main objection to the use of large doses of opaque substance is that such doses provoke phenomena of spasm and thus facilitate the immediate entrance of the injection material into Wirsung's duct. This occurrence may lead the surgeon to believe that there are biliary disturbances present. The latter can also be erroneously suspected from the enormous dilatation of the biliary tree which was caused by the injection but which can be wrongly interpreted as being caused by stagnation. Examination of the bile ducts through a fistula or with a T-shaped tube should be even more severely criticized. Choledochotomy, the presence of a tube in the lumen of a delicate duct, the increased pressure, and the large dose of opaque substance in the bile ducts are factors which necessarily disturb the physiology of the ducts and modify their morphology.

Dystonia. In accordance with the hypothetical statement previously made concerning the normal physiology of the hepatocholedochal system, the common bile duct evacuates its contents through the papilla of Vater while in relaxation. Any factor which partially disturbs the contractile mechanism of the papilla produces dystonia, which may be compared with experimental hypotonic stagnation (Westphal) provoked by the contraction of the sympathicotropic portion of the sphincter of Oddi. Quick entrance of the opaque substance (lipiodol) into the duct of Wirsung during operative cholangiography is a clear indication of dystonia. It is possible that in a certain number of cases transient spasms of a dissociated character are not noticeable during the operation because of the lack of reflux into the pancreatic duct, due to the absence of the ampulla of Vater. Cases of this type, under the circumstances, are therefore included in the group of stenosing odditis. In our series 4 per cent of cases were classified as dystonia.

Some investigators (Desplas, Moulonguet, and Malgras) believe that the entrance of an opaque substance into the duct of Wirsung has no pathological significance. They are led to this conclusion because of their method of carrying out the operation: the injection into the gall bladder or into the common bile duct

[1]Although the term "odditis" appears throughout this article the Editors of SURGERY, GYNECOLOGY & OBSTETRICS neither accept nor endorse it as good usage.

of a large dose of the opaque substance with increased pressure, sometimes through a fistula or by means of a drain tube.

The circumstances under which operative cholangiography is performed vary, and one may conclude that the flow of the opaque material into the duct of Wirsung when not caused or provoked by a defective method of injection is far from being a mechanical and passive phenomenon. One is convinced that the flow into Wirsung's duct is an active phenomenon which is caused by the current of the biliary tree flowing into the pancreatic tree. This would seem to indicate that at certain times the current flows in an opposite direction, namely, from Wirsung's duct to the biliary tree. Several factors indicate that the entrance into Wirsung's duct is an abnormal, active phenomenon of pathological significance which might explain the disturbed function (dystonia). Some of these factors are:

1. The unmistakable evidence during observation of the two different phases, namely: in the first phase, total closure of the ampulla of Vater, and in the second phase, partial opening of the ampulla with persistence of the sympathicotropic ring of Oddi's sphincter by which the flow of the opaque substance into Wirsung's duct is permitted (Figs. 1 and 2).

2. The fact that in certain cases the opaque substance may be seen in the first film occupying only the terminal segment of Wirsung's duct and, shortly after, the substance may be observed filling the entire duct (Figs. 3 and 4).

3. The contour of the duct is modified by pre-existing stagnation. The duct looks sinuous, moniliform, and increased in diameter. The fusiform dilatation of the segment of the duct near the ampulla of Vater indicates that the excretory functions of the duct are pathological. The ampulliform aspect of the terminal segment of the duct is the most evident proof of stagnation which, little by little, modifies the architecture of the duct at the part where it opens into the ampulla of Vater (Figs. 2 and 5).

4. The associated lesions and the further progress of the disease, as observed in a group of patients with dystonia, seemed to indicate intimate relations between the two excretory systems. Cholecystitis dissecans, also called exfoliative cholecystitis, was present in 1 case. In another case, the presence of a calculus and reflux into Wirsung's duct were observed during operative cholangiography (Fig. 5). In this case Kehr drainage was applied and the fistula healed well. Later, however, the common bile duct ruptured with consequent choleperitoneum. In other patients not properly treated for stagnation, the crises of pain recurred repeatedly as a result of functional disturbances and the patients had to submit to other operations.

ROENTGEN ASPECTS

Dystonia. The retention of injected material in the pancreatic duct is transient. Within a few minutes, when the sphincter is in complete relaxation, the duct empties its contents at the same time that the contents of the biliary tree are evacuated. The duct of Wirsung in the cholangiograms appears sinuous, dilated, and moniliform, that is, it has a morphological aspect which indicates repeated increased tension on the duct, both because of the stagnation of the pancreatic secretion and because of the reflux of bile. In cases of dystonia, the biliary tree is somewhat dilated, and sometimes elongated and sinuous as a result of biliary stagnation. In some cases, it may be observed that the biliary and the pancreatic trees form, at times, one united system as they meet at the level of the ampulla of Vater.

Inflammatory stenosis of the sphincter of Oddi. Stenosing odditis varies in intensity from simple hypertonicity to complete obstruction of the sphincter of Oddi. The former is comparable to experimental hypertonic choledochal stagnation (Westphal); the latter depends on anatomic factors, such as retractile sclerosis (Del Valle). My personal statistics give an average frequency of 11 per cent.

Stenosing odditis is identified by the stagnation of the opaque substance into the biliary tree 15 or 20 minutes after having been injected into the tree.

The contour of the ampulla of Vater is the most varied. It may be similar to the "sharp

end of a pencil," "hookshaped," or in "the form of the tip of the finger." In most cases a small amount of opaque substance passes into the duodenum. The whole biliary tree, down to the finest intrahepatic branches, appears in the different films throughout the operation. The common bile duct is flexuose, elongated, and of an increased diameter. It is almost always in active peristalsis, as shown by the undulations of its contour. In some cases a general atony of the whole biliary tree may be observed.

In the roentgenograms, the main structures for the excretion of bile present functional and morphologic aspects which indicate their constant strain against the resistance of the sphincter.

RESULTS OF THE DISTURBANCES OF THE SPHINCTER OF ODDI

The functional sphincteral disturbances little by little cause anatomic lesions of the pancreas and of the biliary tree. The cholangiograms in my own files show how frequently lipiodol enters the pancreatic duct, a result especially favored by dystonia. I believe that biliary lithiasis, and particularly the functional disorders caused by the disease, predispose to the development of acute necrosis of the pancreas. The fact that in a large majority of cases chronic pancreatitis is a sequela to biliary lithiasis supports my belief. Dystonia may be revealed by operative cholangiography in 3 per cent of the cases. In many of these cases the roentgenograms reveal the duct of Wirsung in its full extent. Frequently its diameter is increased, a condition which proves that previous stagnation has been present. By means of these operative observations, which prove beyond doubt the existence of functional disturbances in the main excretory route of the bile, it becomes easy to understand how such disturbances favor the entrance of bile into Wirsung's duct. The disturbance in function is sufficient again and again to cause the establishment of communication between the common bile duct and the pancreatic duct. These functional disturbances cannot be felt on palpation nor seen by the eye. And yet, they become so marked that at times the diseased condition of the gall bladder (cholecystitis) is disguised by the associated lesions of the biliary tract and pancreas.

The reflux of bile into the pancreatic tree creates in itself an abnormal condition which is dangerous to the anatomic integrity of the pancreas. The injection of from 30 to 60 cubic centimeters of serum into Wirsung's duct have been considered harmless because they do not cause macroscopic lesions (Estrade). There is no doubt, however, that they do cause anatomopathological lesions from internal trauma, tearing the fine pancreatic ducts and causing foci of glandular necrosis (Brocq).

The most complete statistical records of the past few years show that acute necrosis of the pancreas is a predominant complication of biliary lithiasis—a factor which proves the important relation between the two diseases (Schmieden, 28).

On the other hand, it cannot be denied that a calculus in any part of the common bile duct, especially in the ampulla of Vater, causes irritation which in turn favors spasm. The stone provokes evident dystonia of the sphincter. In several instances calculi have been found impacted in the ampulla of Vater during necropsy in the presence of pancreatic necrosis.

In the Museum of Pathologic Anatomy I saw such an anatomic specimen (Ferraris), which had been taken from the body of an old man who died from pancreatic necrosis. The calculus, the size of a grain of wheat, was impacted in the ampulla of Vater and the sharp end of it entered the lumen of the duodenum.

It is also important to direct attention to the frequency with which acute pancreatic disorders are observed in vagotonic patients. In 48 necropsies following death from pancreatic disease, biliary lithiasis was found in 28 instances. In 10 of these the biliary tree did not show anatomic changes but the history showed justification for a presumptive diagnosis of neurosympathetic disorders (Stocker). All the aforementioned findings indicate the important rôle which the ampulla of Vater plays in the pathogenesis of diseases of the pancreas.

Now then, the functional disturbances which follow reflux of pancreatic ferments evidently play an important part in the evolution of cholecystitis and in the pathogenesis of choledochitis. Certain factors observed in my patients indicate that in some cases pancreatic ferments play an important rôle in perforation of the gall bladder. The reflux of pancreatic juice into the bile ducts is a proved fact. However, it becomes of pathological significance only when it occurs in the presence of sustained blockage of the bile ducts and in association with other factors which activate trypsine. Because of the blockage, a large quantity of pancreatic juice enters into the gall bladder. The vesicular bile, normally acid, becomes alkaline, while at the same time the ferments are activated by the action of the infected bile (Colp, Doubilet, and Gerber, 7).

On the other hand, the fact is emphasized that the peculiar character of exfoliative and dissecant cholecystitis (23) depends on the action of the pancreatic ferments during their reflux into the common bile duct and the gall bladder. The reflux is favored both by dystonia of the sphincter of Oddi and by the great pressure of the juice in the pancreatic tree, which is higher than that of the bile in the biliary tree (Harms).

The general structure of the tunicae of the gall bladder, which constitute the necrotic sac in these cases, can be identified by microscopic study, because of the fact that the changes in the elastic and connective tissues are not marked, notwithstanding the presence of great changes in the structure. This fact, which is of great pathogenic significance, indicates that the lesions are caused by digestive ferments, since the gangrene and suppuration which are caused by infection destroy the tissue structure to such an extent that it cannot be identified, especially if there are vascular lesions which diminish the vitality and resistance of the tissues.

The reflux of pancreatic ferments most likely will play an important part in the production and development of choledochitis. It has been proved by experiments (Westphal) that, besides choledochitis of the necrotic type followed by biliary peritonitis, there can be produced chronic, productive inflammation with destruction of the elastic tissues of the wall of the common bile duct and dilatation of the duct.

HEPATIC DUCT

Before a meeting of the Academy of Medicine of Buenos Aires, which was held October 22, 1937, with Professor B. Houssay as chairman, I presented my observations on the physiopathology of the extrahepatic bile ducts as seen by means of the operative cholangiography. I directed attention to certain phenomena which I had observed and which indicated that there really is a contractile mechanism, namely, a physiological sphincter, at the level of the hepatic duct (20). Normal contraction of the sphincter separates the intrahepatic bile ducts from the extrahepatic branches of the biliary tree at times during normal elimination of bile. However, in the course of diseases of either the intrahepatic or the extrahepatic branches of the biliary tree, the contractile sphincteral functions are disturbed to such a degree that one is justified in establishing the presence of a pathological process in the hepatic duct and its branches.

FUNCTIONAL SYNDROMES

A functional disturbance in the contraction of the sphincter of the hepatic duct prevents synergic action between the duct and other parts of the entire system of elimination of bile. From the knowledge gained by operative cholangiography, it is evident that the disorder of sphincteral contraction is an important factor in the production of pain and of biliary stagnation.

CASE 1. (No. 5 of series 16.) L. F., aged 32 years, was admitted to the hospital in October, 1937. She had had several attacks of typical biliary pain during the last few months before entering the hospital. She exhibited signs of myocarditis for which she had the proper treatment.

At operation a chronic calculous cholecystitis was found. The patent cystic duct in the form of a band crossed the main route of the biliary excretion at the front and opened into the internal border of the retroduodenal segment.

Operative cholangiography was performed. The first film after injection through the cystic duct showed the system of the hepatic duct to be rather dilated and injected. During operation the abnormal course of the cystic duct and the opening of the duct into a segment lower than that in which the

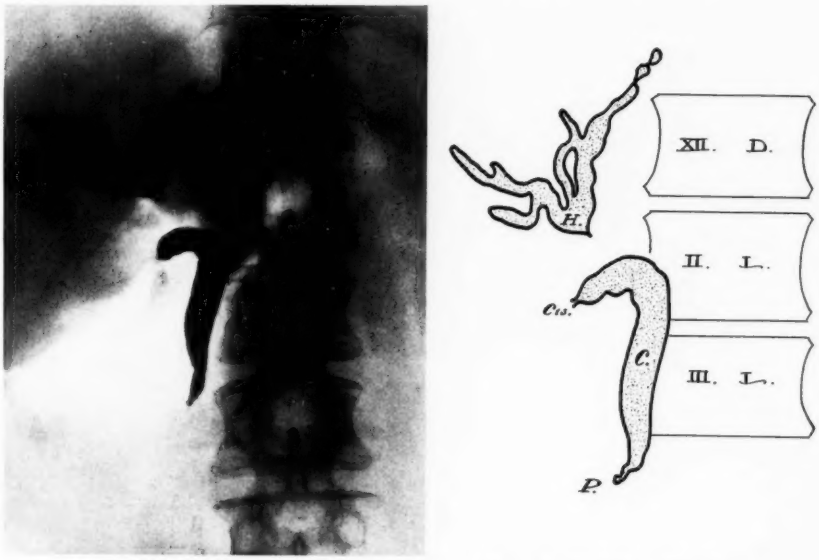

Fig. 1. Dystonia of the sphincter of Oddi. Total closure of the ampulla of Vater. The injection of 3 cubic centimeters of lipiodol was made through the cystic duct, *Cis*. The system of the hepatic duct, *H*, contains lipiodol. The common bile duct, *C*, with dilated and undulated contours does not evacuate its contents into the duodenum because of total closure of the ampulla of Vater, *P*.

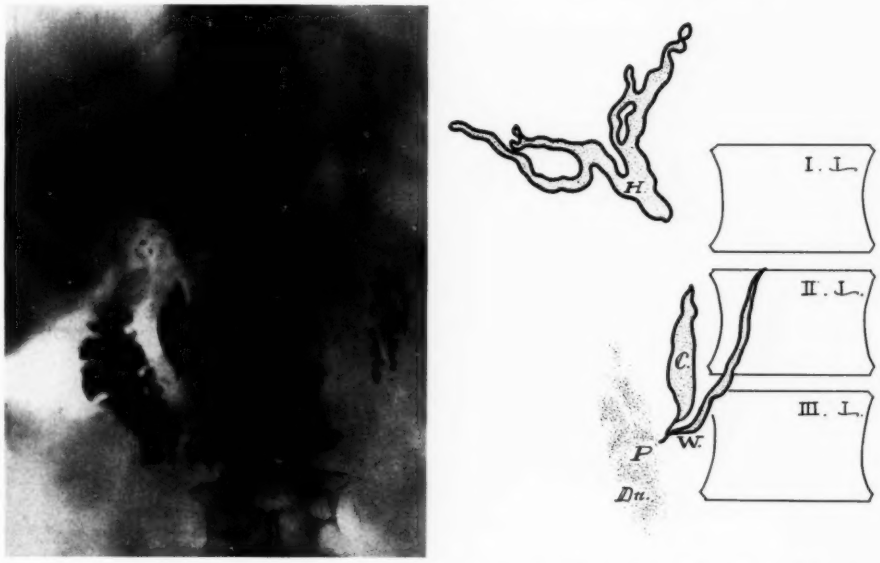

Fig. 2. Roentgenogram of same patient as in Figure 1 taken 10 minutes later showing partial closure of the ampulla of Vater. The system of the hepatic duct, *H*, contains lipiodol. The common bile duct, *C*, has evacuated a portion of its content of lipiodol into the duodenum, *Du*, through the ampulla of Vater. *P*. Lipiodol has flowed into the duct of Wirsung, *W*, the terminal segment of which is ampulliform.

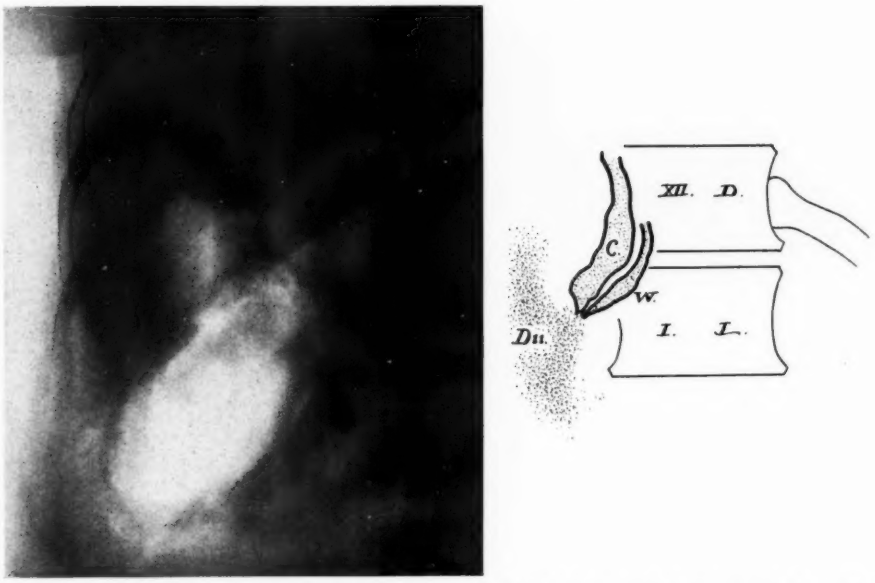

Fig. 3. Dystonia of the sphincter of Oddi. The injection of lipiodol was made into the cystic duct. The common bile duct, *C*, contains lipiodol; Wirsung's duct, *W*, which is injected in its terminal segment, does not show because of its proximity to the image of the common bile duct. A little opaque substance has passed into the duodenum.

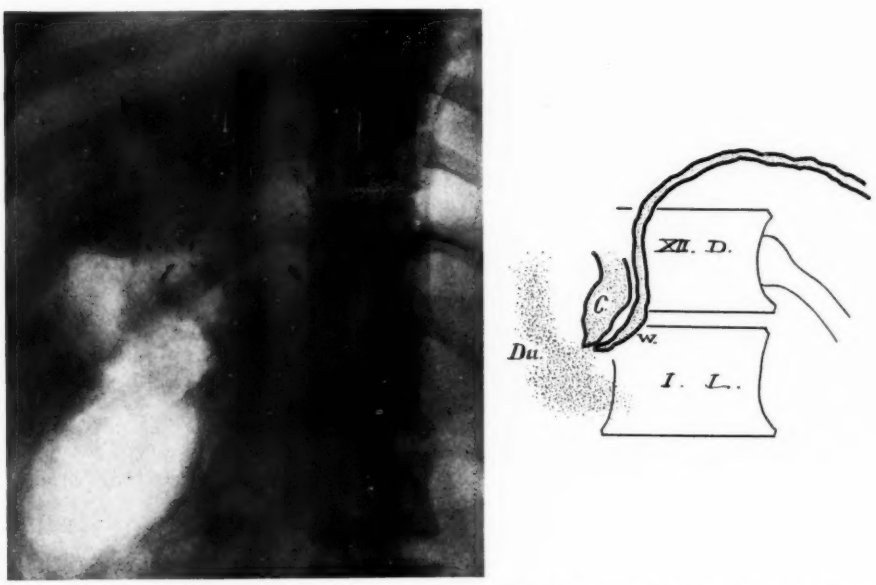

Fig. 4. Roentgenogram obtained 10 minutes later than that in Figure 3. Lipiodol has flowed in greater quantity into the duct of Wirsung, *W*, which is visible in its entirety.

Fig. 5. Dystonia and choledocholithiasis. The injection of lipiodol was made through the cystic duct. The intrahepatic biliary tree is dilated and filled with opaque substance. The terminal third of the common bile duct, *C*, contains a smooth stone, *Cal;* lipiodol has flowed into the duct of Wirsung, *W*, the terminal segment of which is visible, undulated, ampulliform. A small quantity of lipiodol has passed through the ampulla of Vater, *P*, to the duodenum.

duct normally opens were verified. The common bile duct, increased in diameter, was visible. A little lipiodol passed into the duodenum. The second film showed that the system of the hepatic duct was still injected. An accessory hepatic duct was identified. The diameter of the common bile duct was seen to have been reduced and the duct had evacuated almost all of its contents of opaque substance into the duodenum.

The first film indicates that retention of the opaque substance in the intrahepatic branches of the biliary tree depends on the transient action of an active obstructive factor at the level of the hepatic duct. The injection of the accessory duct could be explained by no other mechanism of action than this. The contraction of the upper part of the biliary tree was not sufficient at a given time to overcome the resistance of the contracted hepatic duct. Moreover, it caused reflux of the opaque substance into the accessory hepatic duct which opened above the contracted segment of the hepatic duct. The phenomenon, in this case, is similar to that which occurs when the sympatheticotropic part of the sphincter of Oddi is in contraction from dystonia and reflux into the duct of Wirsung takes place.

CASE 2. (No. 7 of series 43.) C. M. de P., aged 55 years, was an obese multiparous woman. Three years before she had suffered acute pain in the epigastric region, with nausea and vomiting spells. The attack was followed by jaundice and discoloration of feces for about 2 months. The crises of pain recurred at intervals.

Operation was performed May 30, 1940. The subhepatic space was blocked by strong adhesions

Fig. 6. Functional syndrome of the hepatic duct. Roentgenogram taken 10 minutes after the injection. The hepatic duct system, *H*, is completely filled with the substance. Contraction of the distal segment of the hepatic duct (indicated by arrow) is the obstruction. The common bile duct, *C*, of almost normal diameter with repeated peristaltic movements makes lipiodol flow into the duodenum, *D*, through the ampulla of Vater, *P*. The opaque substance contained in the duct of Wirsung, *W*, is visible in the terminal third of the duct.

with the colon and the duodenum. The gall bladder had been reduced to a fibrous nucleus. The findings seemed to indicate that the structure had previously been in communication with the intestine through a fistula which had healed. During dissection the cystic duct had been cut at the level of the common bile duct.

Operative cholangiography was carried out but because the cystic duct was missing it was necessary to inject the opaque substance directly into the common bile duct. The injection had to be made faster than usual because of the reflux of the substance over the lateral surfaces of the cannula.

The injection seemed to cause no signs of dilatation or any anatomic disturbance of the common bile duct because of adhesions between the hilus of the liver and the neighboring structures. Therefore, 8 cubic centimeters of lipiodol was injected, or a dose almost three times that customarily used when the common bile duct is normal. The possible presence of a mechanical obstruction which was produced by calculi or some other cause was kept in mind because of the fact that jaundice had been present for so long a time.

The rapid injection of the large doses caused distention of the biliary tree and spasms. The system of the hepatic duct appeared to be engorged with the substance and the duct was strongly contracted. The diameter of the common bile duct was slightly increased and was peristaltic. The duct of Wirsung was filled with the substance. The ampulla of Vater had relaxed to allow passage of the opaque substance.

In the second film, obtained 10 minutes later, the findings were the same with slight variation; namely, the diameter of the common bile duct was reduced to normal, whereas the hepatic duct was distended above its distal segment which was in marked spasm (Fig. 6).

The results which follow the sudden distention of the biliary tree when the walls of the bile ducts are elastic and irritable are plainly shown by the aforementioned findings. These findings prove also that the circumscribed spasm of the distal segment of the hepatic duct causes more or less prolonged stagnation of the contents of the intrahepatic bile ducts. It is evident then that spasm of the hepatic duct causes slow progressive dilatation of the intrahepatic branches with consequent stagnation—the predominant patho-

genic factor of both transient jaundice and hepatic pain.

Similar phenomena have been observed in several patients with subintrant crises. The distention of the system of the hepatic duct, due to prolonged contraction of the duct which was verified in these patients, was the only explanation for the almost continuous hepatic pain. Neither the gall bladder nor the sphincter of Oddi played any part as causal agents. As seen by operative cholangiography, the gall bladder was in retractile sclerosis and deprived of all its functions of contractility. The cystic duct was obstructed; the sphincter of Oddi did not disclose any obstacle at the level of the ampulla of Vater. Now, by studying by means of operative cholangiography the association between the pathological anatomy and the clinical pathology and the function of the main route of elimination of bile, we have obtained sufficient data to support the statement that the hepatic duct system plays a most important part in the pathogenesis of hepatocolic pain.

Summary and Conclusions

1. The disturbances of the sphincter of Oddi are functional in a great majority of cases. The interference by a permanent, stenosing, anatomic factor are found to be rare.

2. Anatomic stricture of the ampulla of Vater is frequently associated with indurated thickening of the common bile duct (choledochitis).

3. The reflux of lipiodol into the duct of Wirsung is a characteristic roentgenographic finding in the presence of dystonia of the sphincter of Oddi. It represents a pathological phenomenon.

4. Functional disturbances in the sphincter of Oddi in association with reflux into the pancreatic duct are the cause of anatomic changes in both the pancreas and the biliary tract.

5. Functional disturbances in the hepatic duct may occur. In some cases the disturbances are the cause of the development of transient jaundice. The functional disorders of the hepatic duct in association with distention of its branches are quite frequently the pathogenic factors which are involved in hepatic colic.

6. Roentgenograms and clinical proof of my theory stated herein were recently presented (22) in Buenos Aires, with the following conclusion: "In summarizing, *a posteriori*, without divorcing our belief from the general conception of the development, type, and course of biliary pain, it is evident that such a condition in which the factors of obstacle and infection play a rôle in varying proportions (Sprengel) is different in every patient. The degree of intensity varies with the individual because, as Leriche says, pain is like a lamp in an electric circuit, the glow and intensity of its light depending on the intensity of the electric current which passes through its circuit. Therefore there is no doubt that biliary pain, from a pathogenic point of view, is often a functional syndrome of the system of the hepatic duct only to which disturbances of the pancreatic tree, originating in dystonia of Oddi's sphincter, are sometimes added."

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THE TREATMENT OF EXPERIMENTAL SHOCK BY THE INTRAVENOUS INJECTION OF DILUTE, NORMAL, AND CONCENTRATED PLASMA

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THE treatment of traumatic shock demands the restoration of the depleted effective circulating blood volume. Large amounts of fluid and plasma protein are lost from the circulation, and these elements must both be replaced in the relative proportion that they have been lost. When dogs are shocked by intestinal trauma, the fluid which is lost from the peritoneal surfaces contains 3 to 4 per cent protein. This type of shock can be most efficiently treated by restoring to the circulation large amounts of half dilution plasma containing the same proportion of protein that has been lost. Treatment with more concentrated plasma solutions is less effective. The value of half dilution plasma in the clinical treatment of shock has been emphasized in a previous publication (10) and this finding conforms with the experimental results which are being reported elsewhere in the literature.

The widespread recognition of the value of plasma in the treatment of shock has been attested by the numerous publications discussing this subject during the past 2 years. The rapidly accumulating clinical experience, both in this country and in England, has established its efficacy in combating the shock resulting from hemorrhage, trauma, or burns. Plasma finds its greatest value in shock associated with a preponderant loss of the liquid elements in the blood, but it is also of unquestionable value in the emergency treatment of hemorrhage (3). Blood plasma may be preserved in the liquid form for a limited period, or in the lyophile, or dry form, for an indefinite time. The various papers discussing the use of plasma in shock have not been concerned primarily with the concentration to be injected. Alsever has used dilute plasma, but the most commonly used form has been whole plasma. Hill (8, 9) and his coworkers have advocated the use of 4 times concentrated plasma in both the prophylactic and therapeutic treatment of shock. This departure from the more common methods of treatment is strikingly convenient, but depends on the presence of available body water to restore the circulating blood volume.

The recognition that the diminished blood volume is one of the fundamental principles of shock has led to an exhaustive search for the method of its development and the location of the fluid lost. The theory of traumatic toxemia (Cannon) postulates a generalized capillary permeability resulting from a toxic product elaborated at the site of trauma. The importance of local fluid loss at the site of trauma was emphasized by Blalock and by Phemister, who produced shock by traumatizing the extremities of dogs. A tremendous amount has been written since that time, and it is clearly evident that many factors are concerned. These vary from the process involved after a simple hemorrhage from an artery to the complicated mechanism developing after a penetrating wound of the abdomen with minor bleeding. The rôle of the sympathetic nervous system (Freeman), the rôle of visceral capillary dilation (Moon) and that of potassium (Scudder) are all factors in the mechanism of fluid loss, but individually they do not appear to furnish adequate explanation. The increasing information regarding circulatory mechanics, water balance and electrolytes, endocrine dysfunction, and anoxia will eventually be correlated in a more concise understanding of the shock mechanisms.

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TABLE I.—THE BLOOD VALUES IN A CONTROL EXPERIMENT—DOG 40-388, WEIGHT 10.6 KILOGRAMS

	Pl. vol. c.c.	Bl. vol. c.c.	Hematocrit per cent	Specific gravity	Plasma protein concentration per cent	Albumin concentration per cent	Globulin concentration per cent	Total circulating protein gms.
Dog 40-388 Wt. 10.6 kg. Control	890	1520	42.0	1.0267	6.56	2.92	3.64	58.4
2 hr. after trauma	592	1060	44.1	1.0251	5.55	2.33	3.22	32.8
5 hr. after trauma	392	755	49.9	1.0233	5.28	2.35	2.93	20.7
8 hr. after trauma	417	885	52.4	1.0234	5.18	2.22	2.96	21.6

EXPERIMENTAL METHODS

Dogs weighing from 15 to 25 kilograms were used in all of the experiments, and shock was produced by peritoneal trauma under nembutal anesthesia. A typical experiment was performed in the following manner: The dog did not receive food on the evening before, but was given water *ad lib.* On the morning of the experiment it was given .008 gram of morphine subcutaneously, and, half an hour later, sufficient "veterinary nembutal" intravenously to produce narcosis. This method of administration was found to be the most satisfactory because of the great variation in the tolerance of the individual animal to nembutal. The control plasma volume was determined after one-half hour of anesthesia, when the animal could be considered to have reached a basal level. The femoral artery was then cannulated and attached to a recording mercury manometer. The blood pressure tracing was recorded on a smoked drum. Blood samples were taken by jugular venipuncture with an 18 gauge needle without hemostasis except when the venous pressure was very low. The peritoneal cavity was exposed through a midline incision with careful hemostasis. The entire small bowel from the duodenum to the cecum was delivered and gently traumatized with a flat blade retractor. The bowel was held between the fingers and a uniform blow was delivered on the antimesenteric surface. It was necessary to repeat the trauma a second time when dealing with larger dogs. The fluid which exuded from the traumatized bowel was collected extraperitoneally and the bowel was covered with oiled silk to prevent evaporation. Plasma was injected intravenously by gravity, and a Murphy drip bulb was inserted in the system to regulate the flow at 40 to 45 drops per minute.

Blood plasma was injected in three different concentrations, that is, as whole undiluted plasma, as one-half dilution plasma, and as 4

TABLE II.—A COMPARISON OF THE BLOOD VALUES WITHOUT ANESTHESIA, WITH NEMBUTAL ANESTHESIA ALONE, AND AFTER TRAUMA

Plasma volume	Blood volume	Hematocrit	Total protein concentration	Total albumin concentration	Total globulin concentration	Total circulating protein	Total circulating albumin	Total circulating globulin	Remarks
− 6.0	− 7.6	− 3.3	− 8.0	−12.3	− 3.0	−13.5	−17.7	− 9.0	Control without anesthesia
− 7.6	−23.8	−16.5	−11.8	− 7.4	−17.3	−19.6	−22.6	+ 1.4	Control with anesthesia
−55.6	−46.9	+36.8	−21.1	−23.2	−18.9	−66.4 (51.2 gm.)	−67.1 (26.8 gm.)	−65.6 (24.4 gm.)	Shock—intestinal trauma
−29.2	−13.5	+29.5	−25.6	−29.8	−19.1	−47.3 (26 gm.)	−56.8 (19.2 gm.)	−41.6 (8.9 gm.)	Shock—intestinal trauma
−29.7	−15.1	+24.5	− 4.3	− 5.4	− 2.8	−32.6 (18.4 gm.)	−33.6 (10.8 gm.)	−31.3 (7.6 gm.)	Shock—intestinal trauma
−64.4	−41.7	+24.8	−21.1	−23.9	−18.7	−63.1 (36.8 gm.)	−64.8 (16.9 gm.)	−64.5 (20.9 gm.)	Shock—intestinal trauma
−47.5	+43.3	+50.5	− 7.7	− 8.7	− 5.9	−51.5 (34.7 gm.)	−52.0 (23.3 gm.)	−50.4 (11.5 gm.)	Shock—intestinal trauma
−52.4	−32.6	+31.1	−12.1	−7.63	−17.9	−58.1 (54.7 gm.)	−37.3 (20.0 gm.)	−60.9 (24.6 gm.)	Shock—intestinal trauma

times concentrated plasma. The half dilution was prepared by adding an equal volume of normal saline to whole plasma, and the 4 times concentrated by redissolving lyophile plasma in one-fourth the original volume of distilled water. The prophylactic and therapeutic efficacy of these solutions was tested. The prophylactic injection was started coincident with the trauma; the therapeutic injection was not started until the blood pressure had fallen below 80 millimeters of mercury.

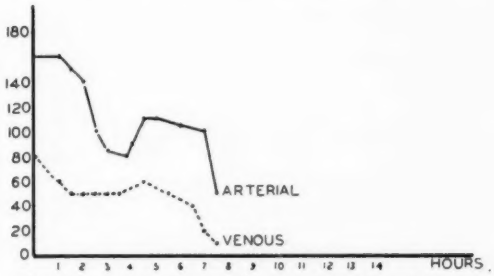
The volume of dilute and whole plasma injected corresponded to the dog's circulating plasma volume. The prophylactic effect of 4 times concentrated plasma was tested with correspondingly large volumes. The therapeutic effect was determined with the smaller amounts which have been suggested for clinical use.

The peritoneal fluid was collected during the experiment and its protein content determined. The animals were killed at the close of the experiment, and sections of the various organs were removed for microscopic study.

Repeated observations were made of the arterial pressure, venous pressure, and circulation time. Blood samples were collected in dry potassium oxalate (2 mgm./c.c. of blood) for determination of the hematocrit, plasma specific gravity, total protein concentration, albumin, and globulin. The circulation time was determined by the sodium cyanide method (4). The protein concentration was determined by the micro-Kjeldahl method, and the albumin globulin ratio by Howe's method. The gravimetric pipette was used in the determinations of specific gravity (4). The plasma volume was obtained by the direct blue dye method of Gibson and Evans, the spectrophotometer being used. Correction for hemoglobin was made. The accuracy of plasma volume determinations may well be questioned when the circulation is failing and the hematocrit is 50 per cent or more. For this reason, only gross changes in volume have been considered significant.

EXPERIMENTAL OBSERVATIONS

The typical reaction of a dog to trauma of the bowel is indicated in Graph 1. There is a primary fall in the arterial blood pressure



Graph 1. Control experiment. Arterial and venous blood pressure in shock produced by intestinal trauma.

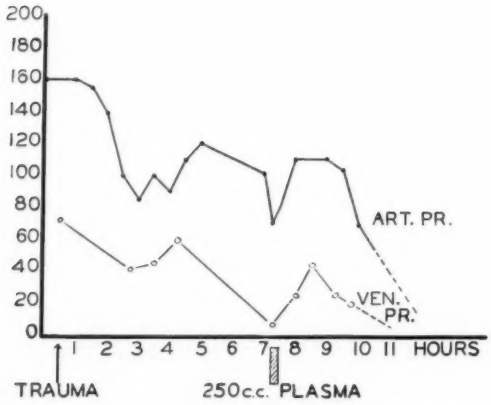
during the first 2 or 3 hours of the experiment followed, in most cases, by a temporary secondary rise. The blood pressure then gradually falls until the animal displays the typical signs of profound shock with peripheral circulatory failure.

The time required after trauma for the blood pressure to fall and the survival time vary considerably in different animals. The survival time averaged 8 hours, varying from 5 to 12 hours.

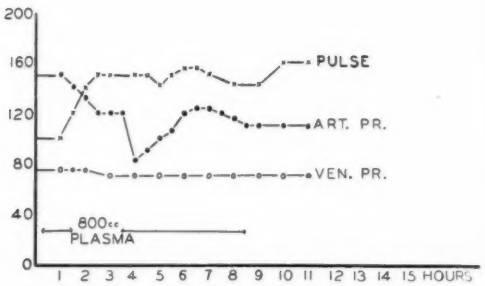
The pulse rate is usually rapid and regular during the early hours of the experiment, but frequently decreases with the appearance of severe shock. The venous pressure slowly declines, and in profound shock it is impossible to withdraw blood from the veins.

The blood findings in a typical control experiment are outlined in Table I. The plasma volume slowly decreases throughout the experiment, with a parallel change in the total blood volume. The change is less marked in the red cell volume calculated from the hematocrit, which indicates a retention of cellular elements in the presence of escaping fluid. The red cell hematocrit becomes concentrated as the shock develops. The specific gravity of the plasma decreases. The concentration of the circulating total protein uniformly falls, and there is a marked decrease in the total circulating protein. The circulation time increases as the arterial and venous pressures decline. The fluid which exudes from the traumatized bowel is serosanguineous and has a protein content varying between 3 and 4 grams per 100 cubic centimeters.

Dogs have been studied without anesthesia, with nembutal anesthesia alone, and with



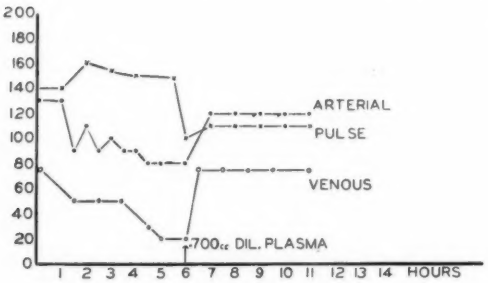
Graph 2. Therapeutic effect of whole plasma. Dog 40-180.



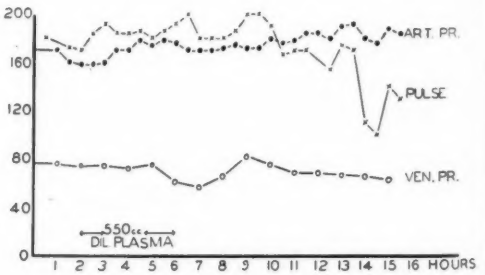
Graph 3. Prophylactic effect of whole plasma. Dog 40-271.

anesthesia plus trauma. The blood and plasma volumes, the hematocrits, and the protein determinations are tabulated in Table II. The first two groups represent the average percentage changes in groups of experiments; the results in the shock group are tabulated individually. The most striking change noted in the shock group is the very marked fall in the circulating protein which varied from 32 to 66 per cent of the original content. These results correspond to the decrease in the plasma volume, but are accentuated by the fall in the concentration of the circulating protein. The protein concentration has never increased in this type of shock. Nembutal anesthesia produces a dilution of the hematocrit in the normal dog due, in part, to stagnation of red cells in the spleen. The hemoconcentration present in shock is very striking because of the dilution in the control.

Shock treated with whole plasma. The injection of whole plasma in the shocked animal results in a temporary rise of the arterial and venous blood pressure. Dog 40-180 exemplifies the usual reaction to whole plasma (Graph 2). The injection of 250 cubic centimeters of plasma raised the blood pressure from 60 to 110 millimeters mercury. The effect was transitory, and the animal died within 2½ hours. The plasma volume was 965 cubic centimeters immediately following the injection, and within 2 hours decreased to 500 cubic centimeters. The plasma injection caused a temporary dilution of the hematocrit and a temporary rise in the venous pressure. The prophylactic effect of whole plasma is indicated by the reaction of dog 40-271 (Graph 3). This dog received 800 cubic centimeters of plasma beginning at the time of trauma. In this type of experiment plasma does not prevent the initial fall in blood pressure, but tends to stabilize it above



Graph 4. Therapeutic effect of dilute plasma. Dog 40-202.



Graph 5. Prophylactic effect of dilute plasma. Dog 40-274.

TABLE III.—THE EFFECT ON THE BLOOD VALUES OF HALF DILUTION PLASMA INJECTED THERAPEUTICALLY AND PROPHYLACTICALLY

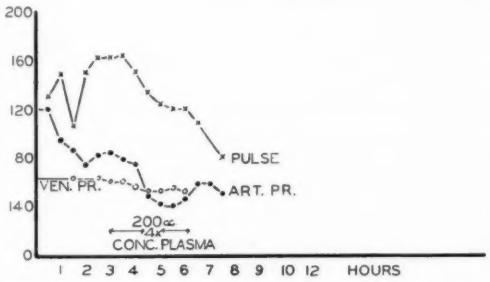
	Plasma volume c.c.	Hematocrit	Total protein concentration	Total circulating protein gm.	
Dog 40-202	805	53.9	6.86	55.0	Control
Therapeutic injection	570	69.8	5.10	29.0	Shock
	950	45.3	5.06	48.0	After plasma
Dog 40-274	570	59.6	5.45	31.1	Control
Prophylactic injection	690	52.7	5.03	34.7	4 hr. after trauma
	645	65.7	4.62	29.8	12 hr. after trauma

the shock level. At the end of 12 hours the arterial pressure remained at 110 millimeters of mercury, and the venous pressure was within normal limits. The large amount of plasma maintained the plasma volume at a constant level throughout the experiment. The hematocrit did not change during the plasma injection, but gradually increased after the injection.

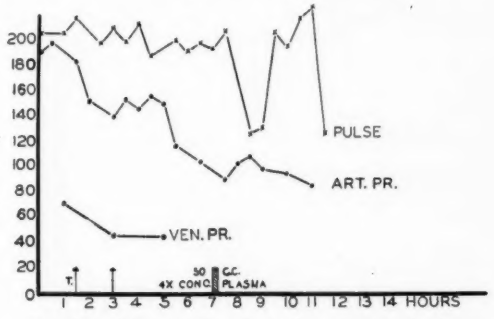
Shock treated with half dilution plasma. Large amounts of dilute plasma will restore the circulation of the shocked dog to an approximately normal condition (Graph 4). Dog 40-202 received 700 cubic centimeters of dilute plasma, the plasma volume was increased to the normal level, and the hematocrit decreased. The blood pressure returned to the control level, and the venous pressure increased to within normal limits.

Injection of dilute plasma gives the most uniform response of all the concentrations tested. Dog 40-274 (Graph 5) was given 550 cubic centimeters of half dilution plasma starting immediately after trauma. The arterial and venous pressures, as well as the plasma volume, were maintained at the normal level for 16 hours. The dog's general condition seemed excellent at the end of this time, but the experiment was terminated by sacrificing the animal. The results in 5 experiments have been similar to that of dog 40-274. Table III illustrates the effect of dilute plasma on the plasma volume, hematocrit, and total circulating protein.

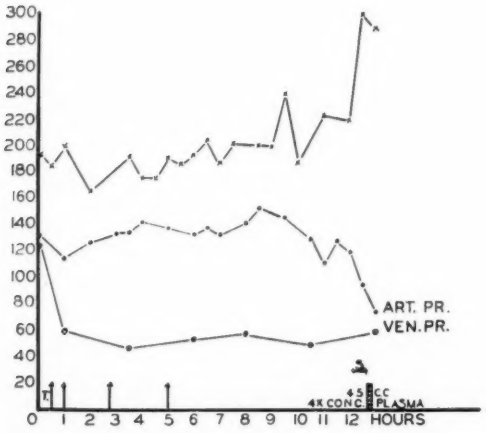
Four times concentrated plasma. The effect of injecting a relatively large quantity of the concentrated plasma is illustrated in Graph 6. Dog 40-341 received 200 cubic centimeters with no appreciable effect on the arterial pressure. The venous pressure was fairly well maintained until death. The plasma volume decreased from 774 to 400 cubic centimeters 1 hour before death. In this type of experiment the plasma specific gravity and the plasma protein concentration increase as would be anticipated. The therapeutic effect of the concentrated plasma is apparently variable as an occasional dog did survive longer than dog 40-341. In an occasional experiment of this type, the plasma volume would remain essentially unchanged during the injection, but



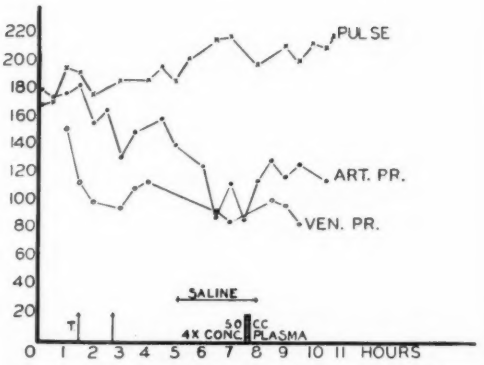
Graph 6. Prophylactic effect of concentrated plasma. Dog. 40-341.



Graph 7. Therapeutic effect of concentrated plasma. Dog 41-15.



Graph 8. Therapeutic injection of concentrated plasma; 45 cubic centimeters of saline given by stomach tube. Dog 41-16.



Graph 9. Therapeutic injection of concentrated plasma; 50 cubic centimeters of saline injected subcutaneously. Dog 41-193.

in spite of this the blood pressure fell, followed by the death of the animal.

Four times concentrated plasma has been injected intravenously into an animal with peripheral circulatory failure. If the amount used is comparable to the quantity which has been used in a patient suffering from shock, the effect on the blood pressure, venous pressure, and on the dog's general condition is negligible. Repeated experiments (6) have produced the same negative result, as demonstrated in Graph 7.

The use of four times concentrated plasma does not supply available water to replenish the depleted circulating plasma volume. Graph 8 represents an experiment in which the dog was given water by stomach tube when the blood pressure was 70 millimeters of mercury. The concentrated plasma was then injected intravenously, but the circulation was not improved. It must be admitted that in this type of shock the absorptive surface of the bowel has been damaged by trauma, hence this may not be a fair trial of the oral administration of water supplemented by concentrated plasma.

The type of experiment in which concentrated plasma seemed to have a beneficial effect on the blood pressure is shown in Graph 9. The dog was given saline solution by subcutaneous injection when the blood pressure was falling. When the pressure had reached 70, concentrated plasma was injected. This was followed by a temporary improvement in the circulation.

ANALYSIS OF RESULTS

The type of peripheral circulatory failure produced by peritoneal trauma conforms essentially with that produced by the usual experimental methods. This is characterized by a fall in the arterial and venous pressures, a decrease in the plasma volume, and a concentration of the hematocrit. The plasma protein concentration uniformly decreases. This is not in agreement with the more generally accepted concept of protein concentration, but does agree with the observations of Dunphy, who found a decreased concentration in experimental burnshock. The most striking feature is the very marked decrease in the total circulating protein, which raises the intriguing problem of determining its fate. A considerable amount can be recovered in the peritoneal exudate, but at the present time it is not possible to state the proportion lost by this route. The data suggest that there is also a general loss of protein throughout the body, but the experimental evidence is not conclusive. This will be discussed in a future publication.

The results indicate that dilute plasma is more efficient than concentrated plasma in the prophylactic or therapeutic management of experimental peripheral circulatory failure. The intravenous injection of large volumes of

one-half dilution plasma have prevented the development of shock. Whole plasma has a similar effect. The results obtained with the concentrated plasma are at best unpredictable, and are not comparable to those obtained with either of the other forms.

The fluid which is lost from the bowel contains 3 to 4 per cent protein, and it seems logical that both fluid and protein should be replaced in the same proportion. Theoretically, the injection of four times concentrated plasma might increase the plasma volume by withdrawing fluid from the tissue spaces. This assumes that such fluid is readily available. The results of these experiments indicate that with the peripheral circulatory failure of shock this extravascular fluid cannot be reclaimed in effective amounts by the use of hypertonic solutions. Fluid must be made available by parenteral injection or concentrated plasma injections will only add to the already increased viscosity of the blood. The increased efficiency of the concentrated plasma supplemented by a saline hyperdermoclysis supports this contention.

It should be emphasized that it is extremely hazardous to compare experimental results with conditions which occur in clinical practice. The type of shock studied in the laboratory is severe, and very large amounts of plasma are required to be effective. However, large amounts of dilute plasma have been useful in preventing operative traumatic shock (10). The experiments also indicate that very large amounts of plasma may be necessary in treating the patient. This has also been emphasized by Dunphy and others. If the circulating plasma volume of a patient is depleted to 50 per cent of its normal amount, the usual 500 cubic centimeter transfusion would be extremely inadequate in treatment of the profound shock. A logical argument in favor of the concentrated plasma is that clinically one deals with a well hydrated individual who has rapidly developed shock following an injury. Also that the four times concentrated material might modify the factors leading to circulatory failure until the injury can be adequately treated. This can only be determined by extensive clinical trial.

Experimentally supporting evidence has not been found. It appears unlikely that fluid can be reclaimed by hypertonic plasma after shock has become established.

SUMMARY AND CONCLUSIONS

1. Experimental shock has been produced by intestinal trauma. This type of shock is characterized by a reduction in the circulating plasma volume, a concentration of the hematocrit, a decrease in the plasma protein concentration and specific gravity, and a marked decrease in total circulating protein.

2. The therapeutic and prophylactic value of half dilution plasma, whole plasma, and four times concentrated plasma in treating experimental shock has been compared.

3. Large amounts of half dilution or whole plasma are more efficient than concentrated plasma in this type of shock.

4. The large amount of protein lost from the circulation has been emphasized.

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THE ENDOCRINE ASPECTS OF CHRONIC MASTITIS

Further Report on Rates of Estrogen Excretion and Results of Hormone Therapy

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FROM a wealth of clinical observation and laboratory experiment, it is now known that the proliferation and atrophy of the epithelial and certain of the connective tissues of the breast depend upon the rise and fall in the function of several endocrine glands. The internal secretions of the ovary are, in fact, essential for the very existence of the mammary gland as an active organ. Since breast tissue is clearly a prerequisite for the development of chronic mastitis, the hormones which maintain the breast in this state are also necessary factors. Regarding this point there can no longer be any disagreement. Yet, in spite of much discussion of chronic mastitis as an endocrine disease, no one has yet succeeded in proving that this breast condition represents a specific response to any recognized type of glandular dysfunction.

The first step toward the solution of the problem of chronic mastitis is the establishment of what constitutes the essential tissue change taking place in the breast. In particular, it is necessary to consider if chronic mastitis is not actually a collection of several diseases, each with a distinctive morphology and each with a special set of causative factors.

CLASSIFICATION OF CHRONIC MASTITIS

Most classifications of chronic mastitis have been based on small histological sections from surgical specimens in which rather localized processes, such as cysts or papillomas, attain an exaggerated importance. In considering this disease from a functional standpoint, however, it is necessary to regard the breast as a whole and to base a classification on clinical characteristics, on the gross examination of tissue, or on the study of histological sections taken outside of areas of circumscribed neoplastic activity.

From our study based on such criteria, it has appeared that there are easily distinguishable two major types of breast reaction to what might prove to be endocrine agents. (a) In the first type there may be only premenstrual pain and swelling, but usually there develops also a tender nodular induration of the outer quadrants. Gross section of such breasts reveals a dense, shining white fibrous tissue. (b) In the second type there is a milky or oily secretion from the nipple with perhaps some palpable dilatation of the large ducts beneath the areola. Section reveals dilated tubules of all sizes from which may be squeezed a grayish white or brown fluid material. In previous studies efforts have been made to determine the histological basis of these two clinical types (66) and the nature of the surgical lesions arising in them (69).

TYPE 1. The histological changes in the breast in which there is only pain and premenstrual swelling are difficult to evaluate because of a dearth of surgical material from such cases. In a few sections studied there appeared to be only a loosening of the periacinal connective tissue, suggestive of an increase in interstitial fluid in that area (Fig. 1). This appearance has been described as a premenstrual "edema" of the periacinal connective tissues and referred to by several writers. The condition of simple premenstrual pain and swelling seems, however, to pass directly into the next stage in which clinically detectable changes in breast structure are present.

In the breast with diffuse outer quadrant induration the most striking histological

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change was found to be a connective tissue proliferation, which distorted the gland fields, compressing and scattering the small ducts and acini (Fig. 2). In many cases, however, it appeared that there was also a proliferation of acini, giving a morphologic structure resembling adenomyosis of the uterus (Fig. 3). As an accurate description of the process in the breast and to bring the terminology into harmony with that used in the pelvis, the term *adenofibrosis* for this variety of chronic mastitis seems most fitting. Semb in his exhaustive pathological study of chronic mastitis adopted the term "fibroadenomatosis" indicating a conception of morphology of the disease very similar to the one here presented.

TYPE 2. In the breast with secretion from the nipple (Fig. 4) there was found dilatation of the ducts with amorphous material and desquamated cells in their lumens. Periductal edema with collections of lymphocytes was a common finding, but diffuse fibrosis was absent. The pathological process in this condition evidently takes place in quite different components of the breast structure from that in adenofibrosis and leads to correspondingly different morphologic results. Clinically this condition may be called nonpuerperal lactation or galactorrhea, but in its pathological aspects it appears as duct dilatation with stasis of secretions.

With both types of breast disease the areas selected for surgical excision contain, as might be expected, more complicated types of epithelial hyperplasia (Figs. 5 and 6). These no doubt constitute the practical therapeutic problems, but it has been the concentration of attention on these localized, but perhaps only secondary, manifestations of epithelial activity that has caused some neglect of the generalized breast changes that might permit the study of some constitutionally effective etiologic agent.

POSSIBLE FACTORS IN THE ETIOLOGY OF CHRONIC MASTITIS

Before the enumeration of the endocrine aspects of these two types of chronic mastitis it will be useful to consider two hypotheses which are, at least for the moment, tenable in regard to their cause.

1. According to a currently popular view, the cause of chronic mastitis is an excessive, prolonged, or unbalanced endocrine stimulus acting principally on the epithelium. Hyperplasia of the ducts and acini of the breast could, for example, be expected to result from stimulation by the estrogens; abnormal secretion, from an anterior pituitary hormone or the sudden withdrawal of an ovarian hormone. If this concept were correct, chronic mastitis would be the actual equivalent of conditions produced in the laboratory by the injection of various endocrine substances.

2. The breast is, however, also subject to effects produced through disturbances in its nervous and vascular systems. The rapidity with which the premenstrual swelling of the breast develops each month can indeed only be explained on the basis of a vascular reaction with an increase in the fluid content of the mammary tissues. Such a fluid increase may be due to the ovarian hormones, which are known to cause a general fluid retention (70) as well as a concentration of fluid in certain portions of the reproductive tract (4, 5, 78). Vascular change may also be initiated through the nervous system, as shown in recent experiments on the mammary blood volume of cattle (59) and in reported examples of sudden increase in the size of the human breast after psychic stimuli (67).

That permanent organic change in breast structure may be the result of an alteration in the chemical environment of the cells, caused by local vascular disturbances, is an easy hypothesis to offer, but difficult to prove. Chronic congestion has, however, been held the cause of pathological effects in various parts of the body, but particularly in the organs of reproduction. In the female it has been held responsible for the sclerotic and cystic ovary (33), for adenomyosis of the uterus (48) and for the so-called chronic parametritis (28); in the male for prostatic hypertrophy (41). Adenofibrosis is a disease arising in a related organ with morphologic features very similar to those of adenomyosis and prostatic hypertrophy.

At least two theories must therefore be considered for the etiology of chronic mastitis. The first asserts that the condition is the

result of abnormal stimulation of the breast, particularly of the epithelium, by one of the ovarian hormones. The second view suggests that as a result of nervous and perhaps endocrine stimuli the breast becomes the seat of chronic or repeated vascular congestions, producing conditions that lead eventually to a fibrosis or an adenofibrosis in which later secondary epithelial changes of all sorts may develop. The evidence for these two conflicting views will be taken up under five principal headings.

CLINICAL CHARACTERISTICS OF CHRONIC MASTITIS

The symptoms and signs of the two types of chronic mastitis give the clinician at once some indication of the nature of the conditions.

The pain and swelling, which are such important aspects of *the adenofibrosis type*, have been ascribed by some writers to the premenstrual proliferation of breast epithelium (55) and by others to the distention of the ducts with desquamated cells (14). Actually there is little morphologic evidence either for a cyclical proliferation or cyclical desquamation of human breast epithelium. It seems almost certain, on the other hand, that the premenstrual tension of the breast with its associated tenderness is due to a regularly recurring vascular engorgement or increase in interstitial fluids. Pain on this basis would of course be increased when fibrosis of the breast is present and the premenstrual swelling of the susceptible periacinal tissues must take place within a relatively unyielding fibrotic stroma. If an analogy is to be made with the symptoms of any pelvic condition, it must be with the congestive type of dysmenorrhea, with its characteristically premenstrual discomfort or perhaps with adenomyosis and endometriosis. None of these is now regarded as essentially an endocrine disease.

Secretion from the nipple is, however, a symptom which points in a rather different direction. The source of some nipple discharge is undoubtedly local, as in the instance of serous fluid coming from a duct containing a papilloma. In cases in which there is a milky secretion from many ducts of both breasts or a discharge of semisolid, fatty material, the functional response of the breast to its natural, endocrine stimulus is closely imitated. Here then an endocrine cause seems likely from the clinical findings.

COMPARISON OF THE HISTOLOGY OF CHRONIC MASTITIS WITH BREAST CHANGES EXPERIMENTALLY PRODUCED BY HORMONES

The second point concerns the many attempts to reproduce the disease in animals by the administration of endocrine substances. With the injection of various hormones, especially the estrogens, pathological proliferation of the epithelial elements in the mammary gland certainly occurs (9, 29). Some workers have insisted on the similarity, if not identity, of these induced tissue changes with those of the spontaneously developing chronic mastitis of women (11, 35, 36, 37, 38). This question of course strikes at the root of the problem, because if the laboratory lesions are the same as those found in human chronic mastitis, the cause of the latter disease is already known. If they are different, new factors or an entirely new hypothesis must be sought.

A systematic attempt to compare the histology of chronic mastitis with the lesions artificially produced in animals by hormone administration was recently made at the Memorial Hospital (69). Sections from 102 cases of human chronic mastitis were first studied and the lesions tabulated. For comparison the mammary glands of 163 mice that had been treated with one of four different hormone substances were examined. The essential change produced in the mice by estrogen administration was a proliferation of new acini. There was slight epithelial hyperplasia of the duct lining and sometimes dilatation of ducts with desquamation of cells and stasis of secretion. Fibrosis, though reported to occur after hormone administration (2, 16) was a most insignificant feature in our series of animals.

From this study it was concluded that the essential changes of adenofibrosis, which takes place to a large extent in the interstitial tissues, are not identical with those produced in the laboratory by hormone injections (Fig. 7).

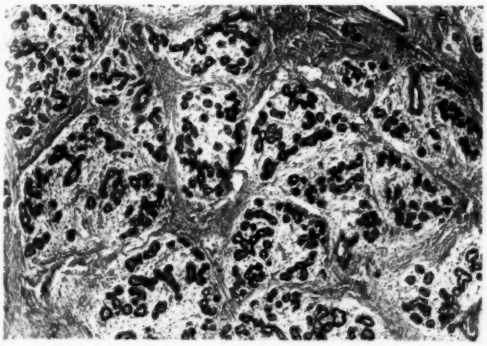

Fig. 1. Intralobular "edema" of the periacinal connective tissue.

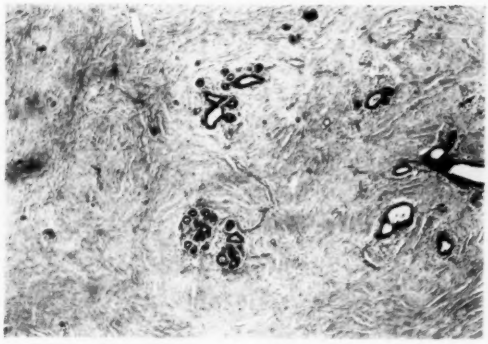

Fig. 2. Adenofibrosis of the breast with fibrosis as the predominant process.

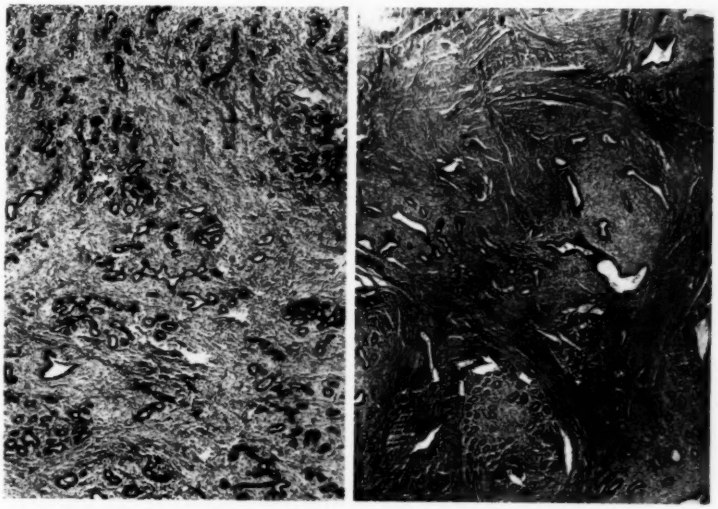

Fig. 3. Adenofibrosis of the breast (left) and, right, adenomyosis of uterus in contrast.

On the other hand, effects somewhat comparable to those found in women with dilated ducts and a non puerperal secretion are producible by these means (Fig. 8).

NATURE OF THE ASSOCIATED DISORDERS FOUND ELSEWHERE IN THE REPRODUCTIVE TRACT

Gynecologic investigation of the patient with chronic mastitis must yield facts of considerable significance, for it is almost certain that any constitutional agent capable of affecting the breast must have its effect on the uterus also. Thus a glandular disorder producing chronic mastitis should cause at least disturbances of menstruation and fertility. On the other hand, were a chronic congestion resulting from nervous or hormone factors prominent in the breast disease, signs of a similar condition might also be expected in the pelvis. From previous articles reporting the gynecologic status of patients with chronic mastitis, four aspects may be selected to stress again (65, 67, 69).

The menstrual history. Disturbances of menstruation certainly affect a minority of women with chronic mastitis. A decrease in

Fig. 4. Abnormal secretion with duct dilatation.

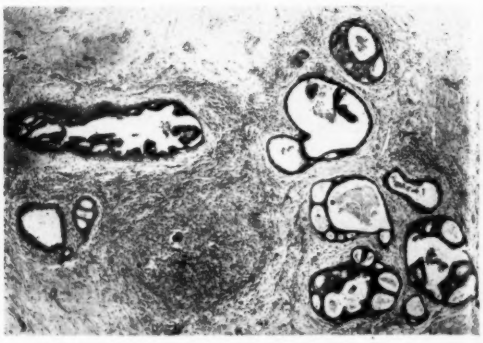

Fig. 6. Localized duct hyperplasias in a case with abnormal secretion.

the amount or duration of the menstrual flow in women with painful breasts has, however, previously been described by at least 7 clinicians (69). From a total of 261 patients derived from two series of published cases (67, 69) it is also our opinion that this anomaly of menstruation is significantly more frequent in patients with the engorgement-fibrosis syndrome (adenofibrosis) than in normal women of the same age groups (Table I). The significance of the scant menstruation in these cases is not clear. Beyond the simple fact of the short flow there is little reason to suppose a primary underfunction of the ovary. It is at least as likely that processes taking place in the interstitial tissues of the breast are repeated in the pelvis to cause a local interference with the blood supply in the uterus with a locally conditioned diminution in flow.

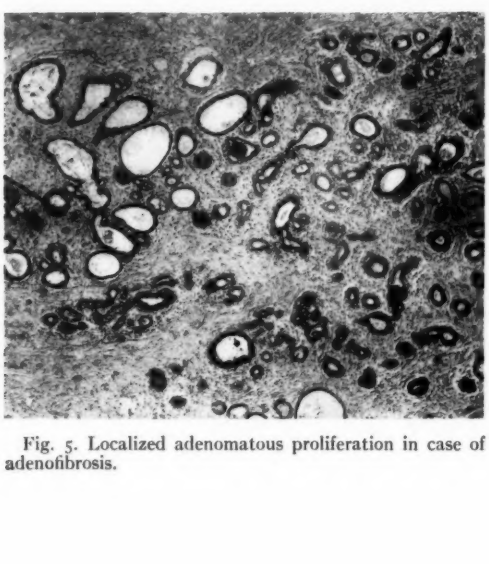

Fig. 5. Localized adenomatous proliferation in case of adenofibrosis.

One point at least in regard to the uterine function of these patients is quite clear. Their endometrial patterns give no indication of any excessive hormone stimulation (67). Perhaps the most popular endocrine hypothesis offered to explain chronic mastitis is that of an excessive estrogenic and a deficient corpus luteum activity. The effects of this type of disturbance on the uterus have long been recognized as a cystic hyperplasia of the endometrium, usually associated with a metrorrhagia. Yet patients with chronic mastitis are not especially susceptible to this disease, nor do gynecologic patients with endometrial hyperplasia show any tendency to the development of breast disorders of this type.

In some contrast to the patients with adenofibrosis, there is among the women with nonpuerperal secretion a high incidence of prolonged menstrual intervals or amenorrhea (Table II). This may in theory be interpreted as the result of a persistent corpus luteum or perhaps of periods of depressed ovarian function during which excessive anterior pituitary activity is released.

Reproductive and lactation histories. In our group of cases about a half of all patients with the adenofibrosis type of chronic mastitis have had no children (Table III), while over 80 per cent of those with nonpuerperal secretion have had full term pregnancies. On the basis of this now fairly considerable series it appears

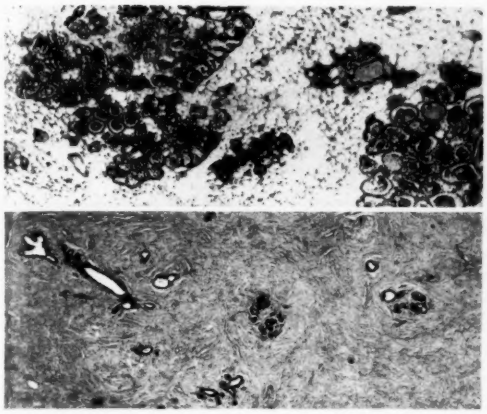

Fig. 7. Estrogen produced acinal hyperplasia of mice, above, in contrast with spontaneous adenofibrosis of women, below.

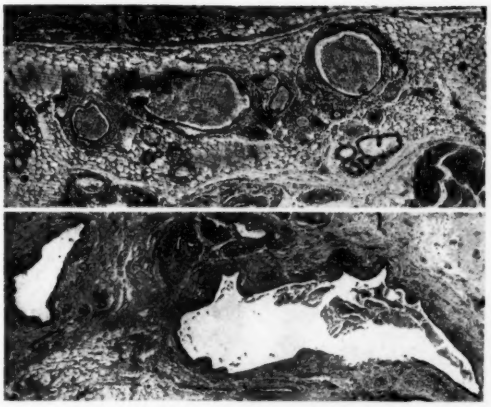

Fig. 8. Estrogen produced duct disease in mice, above, in contrast with dilated ducts containing secretion in women, below.

that adenofibrosis is definitely more common in the unmarried and in those who, though married, have not conceived. The question is open as to whether the failure to bear children led to the chronic mastitis or the conditions associated with the disease predisposed to the relative sterility.

The pathology of the ovary in cases of chronic mastitis. Many of the hyperplastic or neoplastic conditions occurring in the female reproductive tract have been associated by some observer with "cystic ovaries," and among these chronic mastitis is no exception. The functional significance of such ovaries is, however, not known. In one group at least the ovary with small cysts may be quite fibrotic with a reduced rather than an increased function (33). Nothing in the appearance of the ovaries observed during gynecologic operation in women with adenofibrosis of the breast suggests a hyperfunctioning organ (67).

Organic lesions in the pelvis. The cause of breast lesions has frequently been attributed to organic lesions in the pelvis. The most far reaching claims for this viewpoint were made by a former president of the American College of Surgeons, Dr. C. Jeff Miller, who reported the cure of breast conditions following operations for fibroids, for retroversion, and for adnexal disease. Our experience has not been as satisfactory. Of 24 patients with chronic mastitis in whom gynecologic therapy for coincident pelvic lesions was carried out, 8 were apparently cured of their breast disease (65). Since this is about the proportion in whom spontaneous cures or remissions may be expected, it is improbable that such miscellaneous pelvic lesions can be held responsible for breast disease.

Nevertheless, it remains probable, unless chronic mastitis is due to purely local factors, that some equivalent process should be found taking place in the pelvic organs of reproduction. On the basis of a large series of gynecologic examinations it has appeared to us that such an

TABLE I.—DURATION OF MENSTRUAL BLEEDING IN TWO TYPES OF CHRONIC MASTITIS

	Adenofibrosis	Abnormal secretion
Total No. cases	261	93
Normal periods, per cent	75.1	64.5
Short periods, per cent	16.8	17.2
Long periods, per cent	3.8	4.3
Amenorrhea, per cent	4.2	7.5
Menopause, per cent	0	6.4

TABLE II.—MENSTRUAL CYCLE IN TWO TYPES OF CHRONIC MASTITIS

	Adenofibrosis	Abnormal secretion
Total No. cases	261	93
Normal cycle, per cent	71.3	44.1
Long or irregular cycle, per cent	13.8	25.8
Short cycle, per cent	9.9	14.0
Amenorrhea, per cent	4.2	7.5
Menopause, per cent	0	6.4
Others, per cent	0.8	2.1

TABLE III.—REPRODUCTIVE HISTORY IN TWO TYPES OF CHRONIC MASTITIS

	Adenofibrosis	Abnormal secretion
Total No. cases	261	93
Single, per cent	23.4	5.4
Married no pregnancies, per cent	20.7	7.5
Married miscarriages only, per cent	5.8	3.2
Married with children, per cent	50.2	83.8

associated condition does frequently exist. This takes the form of a disease scarcely referred to in the American literature but widely discussed abroad under the name of chronic pelvic congestion (15) or chronic parametritis (26, 27, 28, 40). According to Freund chronic parametritis begins as a vascular engorgement and, if it persists, ends as a general fibrosis of the pelvic supporting structures. It is interesting that in his patients with chronic parametritis Freund described painful breast nodules, while we have found that nearly a third of the patients with the typical engorgement-fibrosis syndrome in the breast exhibit the broad ligament tenderness so characteristic of the descriptions of chronic parametritis (Table IV). It is possible furthermore that some of the patients with "cystic ovaries," with supposed salpingo-oophoritis and with severe erosions of the cervix belong in this group. Were they added the clinical incidence of pelvic congestion in women with premenstrual breast symptoms might easily reach 50 per cent. It appears then that *a syndrome of which vascular engorgement and fibrosis are prominent features does often occur simultaneously in breast and pelvis.*

ASSAYS OF URINE FOR HORMONE EXCRETION

In a previous study the rates of estrogen excretion and blood level figures on 20 women with various types of benign breast disease were presented (67). No abnormalities were found at that time which could be regarded as characteristic of any group of these cases. At least two records of similar work have been reported since that time. Wanke and Paulsen studied the cycles of 2 cases of "mastopathia chronica" and found a low estrogen excretion. Opposite conclusions were reached by Bucher and Geschickter, who made determinations of the estrogens and pregnandiol in the urine of patients with "mastodynia and adenosis" and concluded that these cases had a corpus luteum deficiency or a relative hyperestrinism.

TABLE IV.—FREQUENCY OF GYNECOLOGIC LESIONS IN PATIENTS WITH CHRONIC MASTITIS

	Adenofibrosis*	Abnormal secretion
No. patients examined	190	44
Chronic parametritis, per cent	28.4	18.1
Cystic ovaries, past or present, per cent	7.9	18.1
Cervicitis, laceration, erosion, per cent	47.9	52.3
Salpingo-oophoritis—past or present—per cent	12.6	6.8
Uterine malposition: prolapse, retroversion 2nd and 3rd degree, per cent	36.8	47.7
Fibromyomas, per cent	11.1	13.6
Previous hysterectomy, per cent	4.2	11.3

*Includes painful nodularity and painful hypertrophy cases of the previous report (67).

Since our report of 1936, 9 further patients have been studied with revised technical procedures. These cases included 3 normal women, 3 with very pronounced pain and engorgement of the breasts and 3 with a bilateral secretion of a milk-like fluid.

Techniques employed in hormone assay. In each case all of the urine excreted during the cycle was collected in 72 hour lots. The original intent had been to determine simultaneously the excretion of total extrogens, of pregnandiol and of gonadotropic substances.

a. The estrogens were extracted with slight modifications according to the method described by Smith and Smith (61, 62). Hydrolysis was carried out first by boiling for 2 hours a 500 cubic centimeter specimen with 40 cubic centimeters of concentrated hydrochloric acid. The urine was then extracted for 48 hours with benzol and the extract, representing a concentration of a hundred times, assayed on castrated white mice. For this purpose 6 spayed mice, primed 8 days previously, were used for each injection level. A reaction was accepted as positive only when 4 of these animals showed fully cornified smears. With such an end point, one mouse unit was equivalent to about .15 gamma of estrone or 1½ international units.

b. Gonadotropic excretion was studied by the method of Levin and Tyndale. This depends upon the precipitation of the hormone with 10 per cent tannic acid and assay of the extract on the infantile mouse uterus. Since other tests were being carried out simultaneously the amounts of urine available for the gonadotropic studies were somewhat too small and accordingly only relatively large quantities were detectable.

c. For the determination of urinary pregnandiol the method of Venning and Browne was followed (72, 73). No melting point determinations were made, since these studies were carried out principally in 1938 when the importance of that step was not evident. For this reason it has not seemed proper

to publish the results on the 80 measurements of pregnandiol that were made. With this reservation it may be stated, however, that no abnormal trends in pregnandiol excretion were evident in the group of menstruating women with chronic mastitis.

Description of results in the 9 subjects studied. Although this work was based on the study of only 9 subjects, the following histories of the 6 with chronic mastitis show that they were in each instance extreme examples of the types of disorder they were selected to represent. Changes in total estrogen excretion, if any exist for these conditions, should have been apparent in such a group.

CASES 1, 2, and 3. These were young, unmarried women without breast or pelvic disease. The menses were normal except that during the study of 1 case, an unexpected delay was encountered. The estrogenic hormone excretion in these cases for the month amounted to 3500, 4600, and 4000 mouse units, respectively. Gonadotropic substance was detected in measurable amounts at the time of ovulation in 2 of these cases.

CASE 4. R. E., admitted September 18, 1937, was a married woman of 29 years with a history of a single pregnancy, ending in a 4½ month miscarriage, 6 months before her admission to the clinic. Menstruation had characteristically been of the 21 to 24 day cycle type with long 7 day periods. Since the miscarriage there had been marked premenstrual breast pain.

The patient remained under observation in the clinic for a year, during which time she continued to complain of severe premenstrual breast symptoms associated with lower abdominal discomfort and backache, dyspareunia, and leucorrhea. A condition of anxiety dependent on home conditions was evident.

Examination of the breasts on several occasions showed them to be medium in size, dependent, very tender with a moderate outer quadrant nodularity. The pelvic examination showed that the fundus was normal in size and position, but with marked tenderness on any manipulation of it. The adnexa and parametria were tender, the cervix hypertrophied with an endocervical discharge.

Hormone assays were carried out, beginning with a menstrual period of June 9, 1938 and ending with the onset of the next period 26 days later. The total excretion of estrogens was 1282 mouse units. No gonadotropic substance was found, but death of the test animals resulted in a failure to get any record of 3 specimens.

CASE 5. J. G., admitted November 11, 1937, was a woman of 28 years, twice married. By a former husband she had had 1 child, now 11 years old, who had been successfully nursed for 7 months. A second marriage of 4 years' duration had been infertile, although no contraceptives were used. Menstrual periods had always been normal, occurring every 28 days and lasting 6 days. A suspension of the uterus had been performed 3 years before admission.

The present illness, having its onset 8 months previously, consisted in a bilateral premenstrual pain and swelling of both breasts beginning 7 to 14 days before each period. Examination showed the breasts to be medium in size, tender with moderate nodularity of the left one and marked induration of the right. Pelvic examination showed the fundus to be normal, a little tender on motion; the adnexa, normal; the cervix, moderately eroded. During the patient's year of observation in the clinic she developed backache, premenstrual pelvic pain, dyspareunia and dysuria. Cystoscopic examination showed only a trigonitis and the urine was sterile.

Hormone assays were begun with the period of April 8, 1938, and continued for 35 days of the cycle. The total excretion of estrogens was 6030 mouse units. Gonadotropic substance was present during 2 three day specimens of the cycle, but these unexpectedly were the days immediately after the menstrual bleeding.

CASE 6. H. J., admitted December 11, 1937, was an unmarried girl of 24 years, whose periods had always occurred at 35 day intervals and been so scant as to be described by her as "negligible." There had always been moderate pelvic dysmenorrhea, but for 7 years there had been in addition very severe pain and swelling in both breasts for 2 weeks before each menstrual period.

Examination showed a rather slender girl with large breasts, diffusely thickened throughout and markedly dense and nodular in the outer quadrants. The breasts were also very tender. No pelvic examination was ever done.

Hormone assays were carried out during the cycle beginning on March 13, 1938. The total excretion of estrogens was 5085 mouse units. Gonadotropic substance was present in the specimen representing the fifteenth, sixteenth, and seventeenth days before the following period.

The patient was later treated with progesterone before her periods receiving 3 units during one month and 15 units the next. Before a subsequent period she received 150,000 units of estradiol benzoate, without affecting the breast symptoms or the amount of menstrual flow.

CASE 7. B. S., admitted January 23, 1937, was a married woman of 38 years, the mother of 2 children, ages 7 and 12. They were each nursed only 1 month on account of painful nipples. The menstrual periods formerly occurring every 28 days and lasting 4 days had stopped abruptly and without apparent cause 3 years before admission. Since that time there had been slight spotting on 3 occasions, but none during the previous year. Flushes had never developed.

For 7 years there had been a discharge from each nipple. Eight weeks before admission there had been a sudden swelling and hardness of the left

TABLE V.—TOTAL ESTROGEN EXCRETION IN NORMAL WOMEN AND IN WOMEN WITH CHRONIC MASTITIS

| Case No. | Type of case | Total mouse units | Average per day | Average estrogen excretion per day in 72 hour periods. Tabulated under days before succeeding menstruation | | |

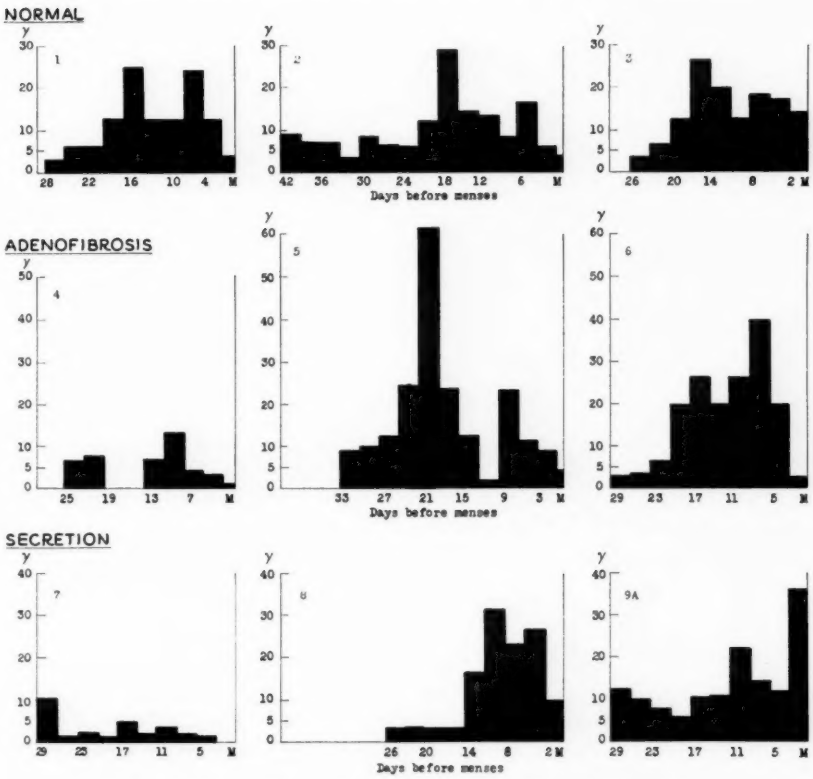

Chart 1. Total estrogen excretion in normal women and in chronic mastitis.

Examination on May 3, 1937, showed the breasts to be medium in size, soft and dependent. From each breast large quantities of milk could be expressed in thin streams. Pelvic examination showed no masses in the pelvis and little evidence of atrophy. The sella turcica was later found by x-ray on July 18, 1938, to be "very small and the posterior sphenoidal process thin."

Four complete sets of hormone determinations were made on this patient (Chart 2). (a) The first, carried out from March 3, 1937, to April 28, 1937, yielded 4,284 units of estrogen. Gonadotropic determinations based only on the microscopic examination of the ovaries gave 1 positive reaction. (b) Beginning May 3, 1937, the patient received 4,000 international units of amniotin 3 times a week for a month. The breasts were unaffected. Determinations of urinary estrogen from May 16 to June 16, 1937, during the period of administration suggested an actual fall in excretion. This month's urine was extracted in duplicate by 2 separate methods using benzol in the Smith and Smith extractor and ethylene dichloride in a simple stirring apparatus. The figures for the two methods were 2,177 and 1,751 respectively. (c) Beginning on June 18, 1937, the patient received 3 injections weekly of 50,000 units of estradiol benzoate for a total of 600,000 units. Estrogen excretion rose to 17,318 units for the 30 days of this study. During this month the breasts were somewhat more swollen and tender than previously, but no diminution in secretion occurred. (d) For a few months after these injections there was little improvement and the patient complained rather bitterly of the breast pain. Then improvement set in. A further set of estrogen determinations made after 14 months and during this period of improvement showed the month's excretion to be 4,074 units, a figure almost identical with that obtained in the first month of study when the abnormal milk secretion was at a maximum.

Summary of results of hormone assays. The results obtained in each of the 115 bio-assays for estrogenic hormone have been tabulated (Table V) and are shown in Chart 1. The specimens in which gonadotropic substance

were found in the urine are also indicated in the table.

Certain points need to be stressed:

The monthly excretion of estrogens for the 3 normal subjects ranged from 3,500 to 4,600 mouse units. Gonadotropic hormone was detectable in 2 of these women at the middle of the cycle. The normal estrogen figures are distinctly higher than those previously reported by us, the difference apparently being due to the additional step of acid hydrolysis. The close agreement of the figures for the 3 normal women is probably accidental and it would be unsafe to consider as abnormal any excretion rate within the range of 1,500 to 6,000 mouse units a month.

The first 2 of the 3 cases of adenofibrosis were married women with symptoms to be regarded as due to an associated pelvic congestion. In each the breast symptoms were of short duration, but in each changes in the texture of the breasts were present. Both women had normal menstrual cycles, and 1 had recently been pregnant. The estrogenic hormone excretion of the 2 showed a wide difference, 1,200 to 6,000 mouse units, in a single cycle. One showed gonadotropic excretion near the time of the menstrual cycle.

The third patient was of a different type, being a single girl who had had scant menses and severe breast pain and swelling since the onset of her periods. No symptoms suggestive of associated pelvic congestion were present. The structural breast changes, almost certainly predominantly fibrosis, were very pronounced. The estrogen excretion was 5,085 mouse units, a high figure, but probably within the normal range. Gonadotropic hormone at the mid point in this cycle might be interpreted as evidence of a normal pituitary stimulus to ovulation.

The 3 cases of abnormal secretion illustrate the extraordinary variety of clinical and hormone conditions under which this symptom may appear. All were in married women who had borne children, but 1 patient was menstruating normally (Case 8), 1 had ceased spontaneously at the age of 35 (Case 7), while 1 (Case 9) had recently undergone a surgical operation with the removal of her uterus and supposedly all of her ovarian tissue. The monthly estrogen excretion in these cases was 900 units, 3,600 units, and 4,300 units, respectively. In none of these were excessive quantities of gonadotropic hormone detectable in the urine.

The third case (Chart 2) deserves special comment for three reasons: (1) The figure of 4,300 units of estrogen excretion is a most unexpected finding in a woman who had apparently suffered the surgical removal of both ovaries. (2) When estradiol benzoate to the amount of 600,000 units was given, the total estrogen excretion in the urine was significantly raised but no alteration in breast symptoms occurred. (3) When, 14 months later, the abnormal breast secretion had begun to diminish total estrogen excretion in the urine was at the same level as that noted when the breast symptoms were at their height. There appeared then to be no correlation between abnormal lactation and estrogen excretion or administration in this extensively studied case.

In judging the significance of these results the general value of urinary assays as a measure of endocrine function needs to be considered. It should be remembered first that when an estrogenic substance is injected intramuscularly as little as 2 to 3 per cent is recoverable in the urine. There is no reason to suppose that the several thousand mouse units of endogenous hormone which appears in the urine during a month's cycle represents any larger fraction of the total amount being produced by that individual. When contrasts of the ovarian function of different subjects are made on the basis of their urinary estrogen the assumption is evidently being made that the excretion rates have a pretty constant ratio to rates of hormone production. There is, however, little justification for assuming that this is true. The possibility that the proportion of effective estrogen, which is excreted, may vary greatly in different individuals, taken with the large error inherent in the technical methods, requires that very large differences in urinary estrogen be present before differences in ovarian function may be claimed. Similar comments must be made about the gonadotropic hormones whose study in the urine of nonpregnant women has been

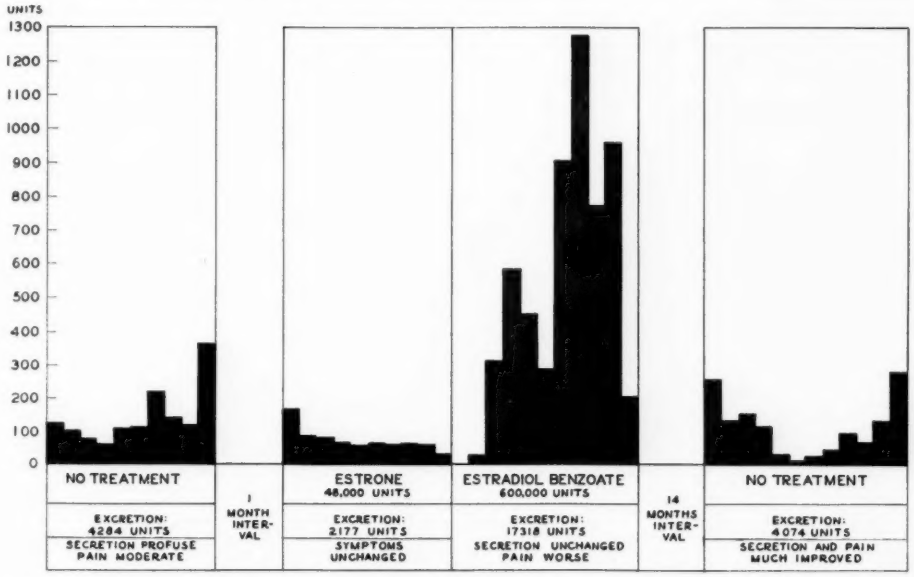

Chart 2. Relationship of estrogen administration to rates of hormone excretion and to symptoms in a case of chronic mastitis.

given considerably less trial than has the estimation of the estrogens. The significance of the absence of the hormone at the time of ovulation or its appearance on unexpected days of the cycle is unknown.

The results show then that in patients with the adenofibrosis type of chronic mastitis a wide range may be found in total monthly estrogen excretion, that the average figure is close to that for normal women, that the extremes are probably within the normal range and that typical peaks of estrogen excretion occur. In 1 case at least gonadotropic hormone appeared in the urine at the expected time for ovulation. Women with breast engorgement and adenofibrosis do not therefore display any characteristic disturbance of ovarian or anterior pituitary function, as determinable by these methods.

In the cases with abnormal secretion from the breast a wide range in the figures for monthly estrogen excretions was present. There was also room for the claim in 2 of the 3 cases that the contour of the excretion curves was abnormal in the sense of an absence of pronounced peaks in estrogen excretion. The failure of large quantities of gonadotropic substance to appear in the urine of the 2 amenorrheic women of the group is of possible interest. Some peculiarities in hormone excretion are therefore present, as might be expected with such pronounced disturbances of menstruation. One cannot, however, on the basis of these studies be precise as to the nature of the hormone disorder in cases of abnormal breast secretion.

THE HORMONE THERAPY OF CHRONIC CYSTIC MASTITIS

The results of endocrine therapy in chronic mastitis is pertinent to the subject, since proof of the effectiveness of such an agent would be strong evidence for the hormone nature of the disease. A review of the history of hormone therapy in breast conditions is a disillusioning exercise.

Chronic mastitis has been treated by each of the new sex endocrines as they became available and, to judge from published reports, all methods have been more or less successful. Substances which have allegedly been followed by improvement include the following: ova-

TABLE VI.—EFFECTS OF NONSPECIFIC METHODS OF THERAPY

	No. cases	Cured	Improved	No change
Gynecologic operation	16	6	9	1
Nonsurgical gynecological treatment	8	2	5	1
Desiccated ovarian extracts	39	7	21	11
Results for 63 cases, per cent		23.8	55.5	20.7

rian residue (20); estrogenic substances by mouth (12, 19, 30, 54); estrogenic substances by injection (21, 32, 42, 75, 77); prolactin (32); corpus luteum by mouth (8, 45); corpus luteum by injection (31); luteinizing gonadotropic hormone (13); and androgenic hormones (3, 22, 23, 25, 34, 46, 52, 63, 64, 71). Opinions on dosage have varied as widely as those on the type of hormone to be used. The "effective" dose of the estrogens has, for example, ranged from the negligible quantity present in the desiccated tablets to over 10,000 units at an injection. Recommended doses of testosterone vary from 10 to 500 milligrams a month.

The physiologic basis for hormone therapy in chronic mastitis. The rationales suggested for the use of the endocrines have been based on conflicting theories of the cause of the disease.

The estrogens were first given because the scant menstruation suggested an underfunction of the ovary (19) and later to overcome a supposed excessive corpus luteum stimulation of the breast (18). Yet such a therapy obviously is given in complete disregard of the known proliferative effects of the estrogens on the breast epithelium of laboratory animals. Certain observations, furthermore, have shown that these substances in sufficient dosage will also produce epithelial growth in the human breast (3, 39). An increase in the tissue fluid should likewise be favored by the estrogens, and swelling of the breasts has been observed to follow clinical treatment (53, 56, 76). Excellent physiological grounds can therefore be found for the statement that the estrogens are contraindicated in adenofibrosis of the breasts.

For nonpuerperal secretion, however, a reasonable basis for estrogenic therapy might be found. Experiment has shown that secretion tends to develop in the mammary glands at the end of a period of estrogenic stimulation and during a time of anterior pituitary activity. It has further been shown—certainly in the laboratory (51, 60) and probably in the clinic (1, 24, 44, 49, 57)—that estrogenic substances will inhibit lactation after parturition. That the estrogens would, temporarily at least, suppress the abnormal nonpuerperal secretion, might at least be hoped.

The use of the androgens or male hormones rests on a sounder theoretical basis. These substances have found a use in a number of gynecologic conditions, such as dysmenorrhea and uterine bleeding, in which their effectiveness seems to be due to an inhibition of the anterior pituitary gland and a consequent reduction in ovarian hormone production. Failure of glandular development and a lowering of the incidence of mammary cancer in mice has been reported to follow injections of testosterone propionate (50). On the other hand, testosterone has also been found effective in suppressing postpartum lactation (6). For these reasons a beneficial effect on either type of chronic mastitis might be expected from male hormone therapy.

Clinical articles on the use of the androgens in chronic mastitis are for the most part uncontrolled case reports and must be accepted with caution. The careful studies of the two English writers, Atkins and Spence, do suggest that some benefit may actually result from giving an androgen in these breast cases. That these effects are temporary and affect little more than the menstrual cycle during which the therapy is given might also be expected and was the actual observation made by Atkins.

Against all other hormones that have been used physiological objections can also be raised. Corpus luteum therapy has been given to correct a lack of balance in the estrogen-corpus luteum ratio but such an "imbalance" has not been demonstrated. The complicated results of the administration of any of the anterior pituitary principles make the effect of their injection on the human breast very problematical. Their influence should, however, be in general one of stimulation and hence probably not to be desired.

The normal course of chronic mastitis. Practically all functional disturbances of the re-

TABLE VII.—TYPES OF HORMONE THERAPY IN 73 CASES OF CHRONIC MASTITIS

		Total cases	Total average dose	Monthly average dose	Monthly range of dose	Average number of months of therapy	Range of months of therapy
Estrone Type 1	Int. units	10	4,700	2,100	450–10,000	2.5	1–4
Estrone Type 2	Int. units	11	46,000	22,500	2,500–60,000	2.0	1–4
Estrone Type 3	Int. units	8	140,000	50,000	2,250–115,000	2.2	1–6
Estradiol benzoate	Int. units	7	301,000	183,000	60,000–600,000	2.8	1–6
Progesterone	Int. units	2	15	6	3–15	2.5	2–3
Gonadotropic luteinizing	Rat units	14	4,590	1,090	600–2,000	4.0	2–9
Lactogenic hormone	Bird units	10	1,440	720	120–720	2.0	1–2
Testosterone propionate	Milligrams	11	350	175	100–350	2.0	1–4

productive organs are characteristically intermittent in their production of symptoms. For that reason all methods of therapy in this field are followed by a certain percentage of apparent improvement. A preliminary estimation of this rate of spontaneous cure or amelioration is essential for the study of any new therapeutic agent used for chronic mastitis, just as it is for dysmenorrhea, amenorrhea, and uterine bleeding.

Two groups of cases are available to us as controls. (a) Thirty cases of chronic mastitis were followed in the clinic without treatment over a 2 year period. At the end of this time a cure or improvement in subjective symptoms was reported by a little over a half (Table X). (b) In a previously published series of 63 cases (65) inactive substances or irrelevant methods of treatment were used (Table VI). This group serves as a particularly valuable control, since the patient had the advantage of confidence in the therapy. Among these

TABLE VIII.—IMMEDIATE EFFECT OF HORMONE TREATMENT IN CHRONIC MASTITIS—RESULTS DURING MONTHS OF ADMINISTRATION

	Total cases	Pain		Nodularity		Secretion	
		Cases with this symptom	Number improved or cured	Cases with this symptom	Number improved or cured	Cases with this symptom	Number improved or cured
Estrone: 3,000 units or less a month	13	13	5	11	2	8	0
Estrone: 3,500–50,000 units a month	11	10	3	10	1	5	1
Estrone: 60,000–115,000 units a month	5	4	2	5	1	2	0
Estradiol benzoate 60,000–600,000 units a month	7	7	1	6	0	3	0
Corpus luteum	2	2	0	2	0	0	0
Gonadotropic luteinizing	14	14	3	14	2	1	0
Lactogenic	10	9	7	10	0	1	0
Testosterone propionate	11	10	8	10	3	3	1
Total for all hormones	73	69	29	68	9	23	2

TABLE IX.—LATE EFFECTS OF HORMONE TREATMENT OF CHRONIC MASTITIS—RESULTS TWO YEARS AFTER THERAPY

	Total cases	Pain		Nodularity		Secretion	
		Cases with this symptom	Number improved or cured	Cases with this symptom	Number improved or cured	Cases with this symptom	Number improved or cured
Estrone: 3,000 units a month or less	13	13	5	11	3	8	2
Estrone: 3,500–50,000 units a month	11	10	3	10	3	5	1
Estrone: 60,000–115,000 units a month	5	4	1	5	2	2	1
Estradiol benzoate: 60,000–600,000 units a month	7	7	2	6	2	3	1
Corpus luteum	2	2	0	2	0	0	0
Gonadotropic luteinizing	14	14	4	14	3	1	0
Lactogenic hormone	10	9	6	10	2	1	0
Testosterone propionate	6	5	3	6	4	3	3
Total for all hormones	68	64	24	64	19	23	8

TABLE X.—RESULTS OF HORMONE THERAPY IN RELATION TO FREQUENCY OF SPONTANEOUS IMPROVEMENT

Type of treatment	Total cases	Pain		Nodularity		Secretion	
		Cases with this symptom	Per cent cured or improved	Cases with this symptom	Per cent cured or improved	Cases with this symptom	Per cent cured or improved
Nonspecific therapy	63	63	78				
Observation only 2 years	30	28	54	28	39	5	0
All hormones: immediate results	73	69	42	68	13	23	9
All hormones: results after 2 years	68	64	37	64	30	23	35

TABLE XI.—HYPOTHETICAL SCHEME OF RELATIONSHIP OF TYPES IN CHRONIC MASTITIS

	Type 1: adenofibrosis	Type 2: duct dilatation stasis of secretion
Stage of functional disturbance	Premenstrual engorgement. Mastodynia	Nonpuerperal secretion Galactorrhea
Stage of diffuse tissue changes	Nodular induration of outer quadrants Fibrosis Adenofibrosis	Duct dilatation Stasis of secretion Periductal inflammation
Stage of localized secondary neoplasia	Types becoming indistinguishable	
	Adenomatous proliferation of the small ducts and acini Cysts	Hyperplasia of ducts Papillomas Cysts
Causative factors	Ovarian hormone Nervous factor Vascular factor	Ovarian dysfunction Pituitary dysfunction

patients about three-quarters reported improvement or cure following their supposed treatment.

The explanation of these somewhat surprising results is simple enough. The pain and premenstrual engorgement are symptoms varying in a given woman from month to month. The patient with this type of breast disease almost invariably applies to a physician in great anxiety at a time of exacerbation of symptoms. It is almost a certainty that from the peak of symptoms which brought the patient to the clinic some amelioration will occur in immediately succeeding months.

It has been our experience, however, that when fibrotic change has developed in the breast to any marked degree, although it may become less painful or even symptom free, some evidence of nodularity will persist almost indefinitely. The secretion of milky or oily material from the nipples is also a condition subject only to gradual change. It lasts as a rule for many months and even well into the menopause.

Effect of injections of various hormones in chronic mastitis. Between 1932 and 1939, 73 cases of chronic mastitis have been treated in the Memorial Hospital Breast Clinic by injections of some hormone preparation.[1] The substances employed included the following: various preparations of estrogens, in doses ranging from less than 3,000 to more than 100,000 international units a month; estradiol benzoate, in doses up to 600,000 units a month; lactogenic substance (prolactin); gonadotropic luteinizing substance; corpus luteum and testosterone propionate. The distribution of cases, the dosage employed, and the effects of the therapy both during and after treatment are given in detail in Tables VII, VIII, and IX.

From a study of Table VIII it appears probable that some improvement in the pain of adenofibrosis occurred during the actual months of administration of testosterone propionate and perhaps also of prolactin. Reevaluation of the cases after 2 years, however, showed that in no hormone group was the improvement in the pain or nodularity significantly greater than in the control series (Tables IX and X). There was indeed a possibility that the estrogens actually retarded recovery, since the proportion of improved cases in the groups so treated was actually lower than could have been anticipated from spontaneous remission alone.

In regard to the symptom of abnormal secretion, one must note that the figures point to an improvement in one-third of the hormone treated cases, 2 years after therapy was given. On the other hand evidence for an immediate effect was slight, a point em-

[1]Although many of these patients were treated some time ago acknowledgement should be made to Dr. Max Gilbert of the Schering Corporation for estradiol benzoate (progynon B) and testosterone propionate (oretone); to Dr. J. A. Morrell of E. R. Squibb and Sons for supplies of estrone (amniotin), gonadotropic luteinizing substance (follutein) and prolactin.

phasized by the failure of 600,000 units of estradiol benzoate to suppress the secretion in Case 9.

Effect of radiation of the ovaries. In contrast to the results obtained when stimulating hormones are employed, are those obtained when the ovaries are removed or radiated. The cases, in which such therapy for breast disease is justifiable, are of course exceptional. Our experience with 18 cases so treated (68) show that pain is invariably cured or improved and the nodularity usually somewhat lessened. Abnormal secretion, on the other hand, is very slightly affected for some time.

Summary on Therapy. From this experience it is our opinion that glandular therapy up to the present time has been of no benefit in the treatment of chronic mastitis. No hormone we have used to date has produced permanent results exceeding the anticipated rate of spontaneous improvement. The estrogens in particular are probably contraindicated in view of their capacity to cause epithelial proliferation and breast engorgement. The androgens and perhaps progesterone may produce temporary improvement by suppressing ovarian function, but there is no reason to suppose that these results will be permanent. The single established fact in regard to hormone therapy is that abolition of the ovarian function by castration will cause cessation of pain in almost all cases of adenofibrosis and a slow but definite disappearance of the nodularity.

SUMMARY AND CONCLUSIONS

In Table XI is presented a scheme of the relationship of different types of so-called chronic mastitis. It is presented as a hypothesis which seems best to explain the facts now available on this subject.

There are two types of abnormal reaction in the breast which appear to be the result of hormonal or other constitutional agents. Each appears in a purely functional stage, but on the basis of each characteristic organic changes may develop.

Type 1 (*adenofibrosis*) is at first characterized only by premenstrual pain and swelling, which seems almost certainly to be due to vascular engorgement or increase in tissue fluids. A diffuse induration of the outer quadrant of the breast due to a proliferation of the connective and epithelial tissues is, however, found in most of these cases and indicates a second stage. A relationship between the excessive premenstrual engorgement and the development of the diffuse fibrosis is suggested by the almost invariable association of the two conditions. Isolated nodules of epithelial activity produce the lumps that require excision but are perhaps purely secondary, localized phenomena developing on the basis of the general adenofibrosis.

Among causative factors it is evident that an actively functioning ovary is a prerequisite to the development of this disease. Yet the infrequency of changes in the cycle of menstruation, the usually normal endometrium, the inability of various workers to agree on any abnormality of hormone excretion and the apparent failure of all endocrine therapy (except castration) speak against any simple quantitative abnormality of sex hormone physiology.

The clinical evidence for an excessive premenstrual vascular reaction in the breasts of these patients is unmistakable and with this are often found clinical signs of a similar disorder in the pelvis. A general nervous instability often with local hyperesthesia of the breast is commonly present in these patients. Many signs point therefore to the need of studying these nervous and vascular factors to determine whether through such agents an abnormal environment may be set up about cells of the breast which could lead to the organic changes of adenofibrosis.

Type 2 (*nonpuerperal secretion*) in its functional stage is characterized by a milky discharge from the nipple and histologically perhaps by slight hyperplasia of the acini. There soon develops a condition in which dilated ducts become filled with desquamated cells and stagnating secretion. That periductal inflammation, cysts, and hyperplastic or metaplastic changes in the duct lining may result when such a condition is of long standing seems probable.

In many cases of this type an endocrine disturbance in the form of grossly disturbed menstrual cycles is quite evident. Atypical curves

of hormone excretion are suggested in 2 cases of this study. Treatment with the estrogens or androgens has a fairly good justification on theoretical grounds but our own results were inconclusive. For these reasons, but principally because stimuli of the hormone type are the essential causes of milk formation, it seems probable that an abnormal milk-like discharge from several ducts has often an endocrine basis.

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I. THE EFFECT OF PLASMA TRANSFUSION UPON THE SERUM PROTEINS AND BLOOD VOLUME OF DOGS RENDERED HYPOPROTEINEMIC BY DIET

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HYPOPROTEINEMIA frequently occurs in patients with lesions of the gastrointestinal tract (8, 12, 16, 20). The coincident edema of the tissues impedes wound healing (23) and diminishes the motility of the small intestine (3). In addition, postoperative edema of anastomotic stomas may so narrow the lumina that signs and symptoms of obstruction will follow (16). The therapeusis of nutritional edema encountered by the surgeon has been directed along essentially two lines of approach, namely: (a) transfusions of fresh or preserved plasma, in the hydrated (13, 22) or dehydrated (lyophile) form (21, 24) and (b) the intravenous injection or transduodenal alimentation of amino acids (8, 21) or proteins (1).

The utilization of transfused plasma protein has been studied in dogs by various workers (6, 11, 19, 25). Weech and his co-workers have shown that the plasma protein concentration of hypoproteinemic dogs cannot be restored to normal by the single injection of massive amounts of plasma (25). Other experimenters have recorded the metabolism and utilization of small transfusions of plasma in fasting (6, 19) and hypoproteinemic (11, 15) dogs and they have demonstrated that the excess protein is not excreted in the urine as urinary nitrogen.

The purpose of this study has been to investigate the effect of plasma transfusions upon the serum proteins and blood volume of dogs rendered hypoproteinemic by prolonged ingestion of a protein-free diet. Studies were made after: (a) single massive plasma transfusions and (b) after multiple small plasma transfusions.

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METHODS

All dogs were given an anthelminthic before experimental procedures were begun. The dogs were fed the essentially protein-free diet suggested by Melnick, Cowgill, and Burack (18) (Table I). This diet was offered in amounts of 70 calories per kilogram of body weight per day.

Plasma volumes were determined by a macro-modification of the method described by Gibson and Evelyn. A uniform dose of Evans blue dye (10 mgm. in 10 c.c. of distilled water) was injected intravenously in all animals regardless of weight. With this procedure good readings were obtained when 1 cubic centimeter of plasma was diluted to 10 cubic centimeters with saline. The K-values for two different lots of dye were found to be 0.144 and 0.147. Following injection of the dye, 5 cubic centimeter samples of blood were withdrawn after 15, 25, 35, and 45 minutes and were prevented from clotting with heparin. Concentration of the Evans blue dye was determined by means of an Evelyn photoelectric colorimeter and the values were extrapolated for calculation of plasma volumes (10).

TABLE I.—MODIFIED COWGILL DIET

Food	Amount per cent	Calories Absolute	Calories Per cent
Sucrose	55.10	220	44.7
Dextrin	18.17	73	14.7
Lard	16.65	150	30.4
Butter*	6.54	50	10.2
Bone ash	2.36	—	—
Salt mixture (26)	1.18	—	—
	100.00	493	100.0

*Butter figured at 7.7 cal-gm-pH-acid to litmus.

Vitamins

Thiamin tablets, containing 0.75 mgm. of thiamin chloride—equal to approximately 250 international units of vitamin B, were given 1 dog, per day.

Liver extract 343 (Eli Lilly) was given in amounts equal to 210 mgm. per kilogram of body weight per day.

Haliver oil, 10 drops, was given once daily.

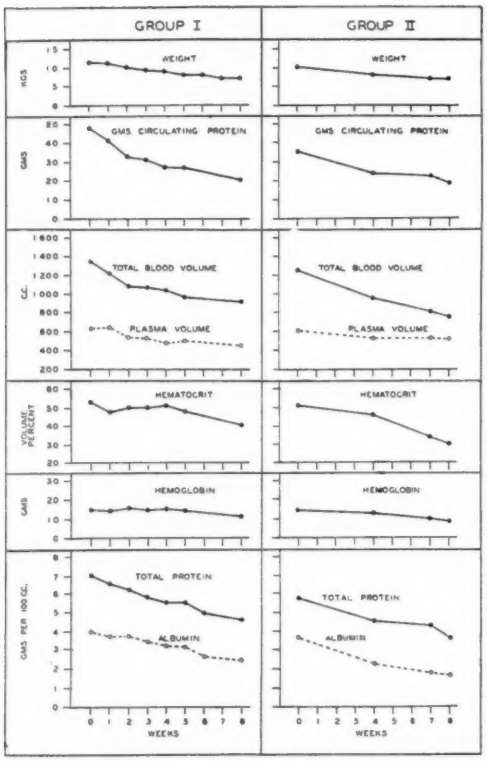

Chart 1. Average changes in weight, total circulating protein, total blood and plasma volume, erythrocyte volume per cent (hematocrit), hemoglobin, total serum protein and albumin fraction concentration in 2 groups of 4 dogs each during 8 weeks on low protein diet.

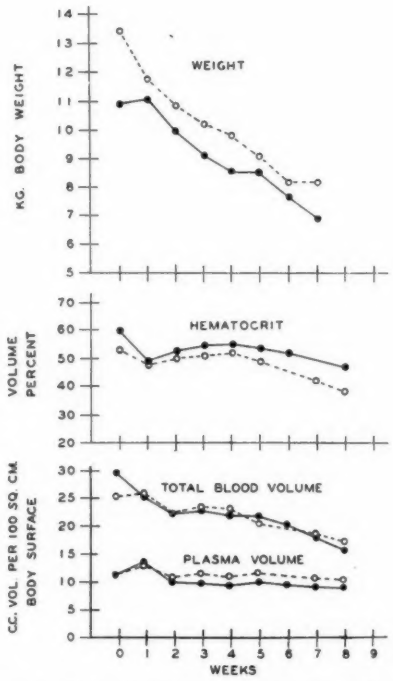

Chart 2. Change in weight and erythrocyte volume per cent (hematocrit) and total blood and plasma volume per unit of body surface in each of 2 dogs during 8 weeks of protein depletion.

Changes in blood volume after intervals of 30 to 40 minutes were calculated from variations in the erythrocyte volume per cent. Hematocrit determinations were made on heparinized blood with the Winthrobe tube.

Serum protein determinations were made by the micro-Kjeldahl procedure. Albumin and globulin were separated by the use of 22 per cent sodium sulphate. Nonprotein nitrogen determinations were made according to the Kock-McMeekin method (7) modified for reading with the photoelectric colorimeter (9). All determinations were made in duplicate.

Blood for plasma transfusions, withdrawn from a group of donor dogs, was prevented from clotting by the use of heparin except in one instance when sodium citrate was used. Plasma, removed by centrifugation and stored in liter flasks at 0 degree to 4 degrees C. until ready for transfusion, was analyzed for total protein, albumin, and globulin concentration. The total serum protein concentration of the pooled donor plasma varied from 5.6 to 6.3 grams per cent.

RESULTS

Effect of low protein diet on blood volume and serum proteins. In order to study the changes in the weight, total circulating protein, total blood volume, plasma volume, hematocrit, hemoglobin, and both the total and the albumin fraction of the protein concentration after the inauguration of the protein-free diet, a group of 4 dogs (group I) was studied at weekly intervals until there was a marked hypoproteinemia. The results are shown in

Chart 1 from which it is noted that there is a gradual decrease in all the values over a period of 8 weeks. It is apparent that the decrease in the total protein concentration is due to the diminishing albumin fraction.

To eliminate excessive bleeding as a factor in the development of hypoproteinemia, another group of 4 dogs (group II) also shown in Chart 1 was studied at monthly intervals. It was found that the development of hypoproteinemia and changes in blood volume were similar to those seen in group I. In 2 dogs (Chart 2) total blood and plasma volumes were calculated on the basis of 100 square centimeters of body surface area (5). The plasma volume decreased slightly with the development of hypoproteinemia and reduction in the absolute plasma volume. By these same methods of calculation the total blood volume decreased proportionately with the development of anemia and a decrease in the absolute plasma volume.

Effect of plasma transfusions on blood volume and blood proteins in hypoproteinemic dogs. Two hypoproteinemic male dogs were given volumes of plasma calculated theoretically to restore the serum protein level to a normal value of 7 grams per cent. The plasma was injected into the jugular vein with a syringe and the entire amount was given in about 10 minutes. These animals were continued on the low protein diet during the period of observation which lasted a week.

The most striking effects (Chart 3) were the immediate but transient increases in the total blood and plasma volumes, both returning to the pretransfusion levels within 3 days. The injected plasma exerted a diluting effect as shown by the hematocrit values. The protein concentration and total circulating protein of the sera showed only a comparatively small rise despite the large amounts of plasma injected.

A study of the serum proteins and blood volumes after small daily transfusions of plasma for 2 weeks was made in 5 hypoproteinemic dogs (Chart 4). Analyses were made at intervals of 18 to 24 hours after the preceding transfusion.

A single daily 50 cubic centimeter transfusion of plasma was followed by a gradual

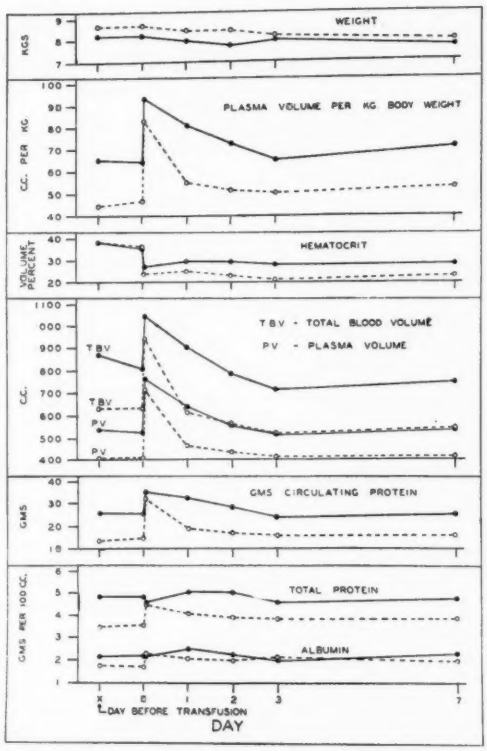

Chart 3. Immediate and late effects of massive plasma transfusion upon plasma volume per kilogram of body weight, hematocrit, total blood and plasma volume, total circulating protein, total serum protein and albumin fraction concentration in two hypoproteinemic dogs. — . — . No. 1, given 220 cubic centimeters of plasma. T.P. = 5.37; A/G = 1.08; o - - - o No. 2, given 215 cubic centimeters of plasma. T.P. = 6.16; A/G = 1.44.

increase in the serum protein concentration in 3 dogs. At the end of the experimental period there were increases of 20, 23, and 58 per cent above the initial hypoproteinemic level. The effect of removal of about 120 cubic centimeters of blood in each animal for analyses during the 2 weeks period cannot be adequately gauged. It would seem that without this withdrawal the actual increase in protein concentrations might have been appreciably greater. The absolute plasma volume showed no change in 2 animals and increased 12 per cent in 1 dog at the end of the experiment. From the percentage concentration of serum proteins and the plasma volumes, it was pos-

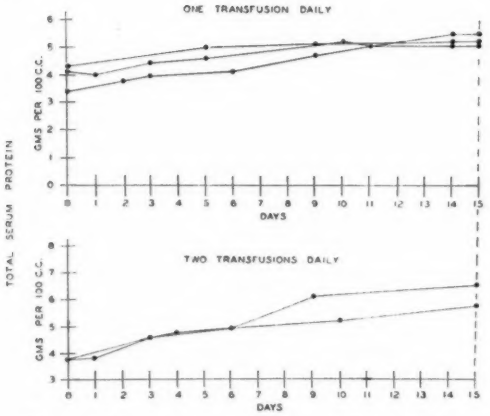

Chart 4. Effect of one or two small (50 c.c.) plasma transfusions daily upon the serum protein concentration of 5 hypoproteinemic dogs.

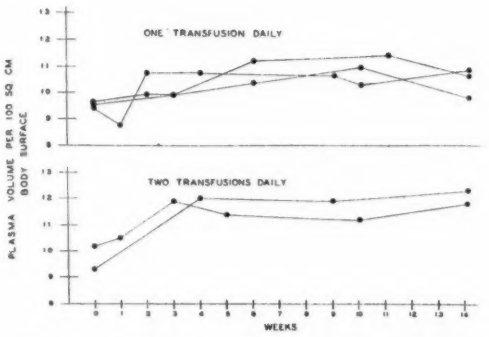

Chart 5. Effect of one or two small (50 c.c.) plasma transfusions upon plasma volume per unit of body surface area.

sible to calculate the total circulating protein; these values were 22, 40, and 60 per cent, respectively, above the pretransfusion levels.

Two hypoproteinemic dogs (Chart 4) were transfused twice daily with 50 cubic centimeters of plasma. The increases in serum protein concentration were 57 and 75 per cent, above the initial values. The absolute plasma volumes of these 2 dogs increased 15 and 25 per cent, respectively. The calculation for the total circulating protein showed that there was an increase of 91 and 137 per cent, respectively, in these animals. The total blood volumes in these 2 groups of animals decreased during the period of experimentation due to the increasing anemia. Plasma volume per unit of body surface increased slightly with the rise in serum protein concentration in both groups of dogs (Chart 5).

EVALUATION OF STUDY

The changes occurring in serum protein in 8 dogs maintained on a protein-free diet are similar to those previously reported by Weech and his co-workers. These investigators described a gradual decrease in the plasma albumin and an accompanying increase in plasma globulin. In the present experiments, it was found that the albumin fraction decreased but that there was no consistency in the behavior of the globulin fraction in the individual experimental animals. The decrease in the albumin globulin ratios was due to the decrease in the albumin concentration rather than to the increase in globulin concentration.

A number of investigators (4, 14, 17) have associated a decrease of the plasma albumin concentration with a proportionate drop in plasma volume. There was no attempt made by these authors to determine the effect of weight loss by correlating plasma volume changes per unit of body weight or body surface. In the present experiments the plasma volume showed only a slight reduction per unit of surface area despite the loss of weight and the decrease in plasma albumin.

Weech demonstrated that the protein concentration of a hypoproteinemic dog could not be returned to normal by a single massive transfusion of plasma. His work has been confirmed in these experiments. In addition, accurate determinations indicated that the blood volumes in these animals were only temporarily increased after transfusions of comparatively large amounts of plasma. From the work of other investigators (2, 19, 27) it appears that plasma proteins can be utilized or stored in animals that have undergone protein depletion. Hence it is not surprising that transfused plasma given in single large amounts did not appreciably increase the serum protein concentration in hypoproteinemic dogs.

Daily single plasma transfusion in small amounts was responsible for a moderate in-

crease in the serum protein concentration of hypoproteinemic dogs. More frequent transfusions (twice daily) produced a marked increase in the protein concentration. Despite the rather marked increases in serum protein concentration, changes in plasma volume, both absolute and per unit of body surface were relatively slight.

SUMMARY AND CONCLUSIONS

1. The protein concentration, total blood volume, and plasma volume were determined in dogs made hypoproteinemic by feeding an essentially protein-free diet. There was an appreciable decrease in the blood protein and volume on such a diet. Plasma volumes calculated on the basis of body surface area also decreased during the depletion period.

2. Single plasma transfusions, calculated to restore the serum protein concentration of these hypoproteinemic dogs to normal, were ineffective.

3. Serum protein concentration was effectively increased by small plasma transfusions given once or twice daily.

4. There appeared to be a relationship between serum protein concentration and plasma volume, both absolute and per unit of body surface area.

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AN EVALUATION OF BLOOD AND BLOOD SUBSTITUTES

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WARS have served as the incentive for many advances in surgery. The uses of blood and substitutes for blood have received particular attention in wartime, and a number of important contributions have resulted. The employment of stored or preserved blood and of plasma was recommended during the last world conflict, but the suggestions did not receive the attention which they merited. These remarks are not meant to imply that the need for blood and its substitutes is peculiar to warfare. The increase in the numbers of operations and of injuries in civil life has extended greatly the indications for the employment of intravenous injections in the prevention and treatment of peripheral circulatory failure. The realization that shock should be recognized and treated in the early rather than in the fully developed stage has resulted in the saving of many lives.

The importance of the subject under consideration is demonstrated by the fact that one of the first of the studies which were requested of the National Research Council by the Medical Corps of the Army and Navy was on the use of blood and blood substitutes. At the initial meeting of this committee more than a year ago Dr. W. B. Cannon mentioned the need for improvements in methods for preparing, preserving, and administering solutions which are already available. In addition, he pointed out the desirability of preparing fractions of blood from man and animals which might be as good as or superior to these fluids. The brilliant work of Dr. Edwin Cohn and his group has resulted already in the separation of human albumen, which for some purposes appears to offer many advantages.

In any choice of a blood substitute one must have clearly in mind the particular function of the blood which requires reinforcement. These functions, all interrelated, may be separated for purposes of discussion. They include oxygen transport by the red cells, osmotic pressure maintenance by the plasma proteins, coagulation through the prothrombin-fibrinogen mechanism, nutrition with special reference to the rôle of the plasma proteins, participation in body response to infection through complement and circulating antibodies, and phagocytosis by the leucocytes.

It is at once obvious that whole blood, and preferably fresh whole blood, is the one fluid which will fortify the circulating blood in the performance of all of its functions. While we shall discuss the relative advantages of given substitutes in various conditions, it must be remembered that in most conditions all substitutes for whole fresh blood are inferior. It is doubtful whether under any but a few special circumstances any of the substitutes is superior to whole blood. Even in the hemoconcentration associated with severe burns the objection to the use of whole blood has probably received more emphasis than it deserves. If the total blood volume is maintained at an essentially normal level, pronounced degrees of hemoconcentration are tolerated remarkably well.

While in a given instance replacement of blood because of disturbance of a single function is the primary concern, several of the functions are probably simultaneously affected. In addition, when dealing with wounded men or with patients on the operating table one must realize that treatment is being given to a person who will not be restored at once to full health. Problems of nutrition, hydration, and infection will have to be met, and the handicapped organism, especially with the additional burdens imposed by wartime conditions, may have difficulty in replacing water, proteins, and perhaps even the formed elements of the blood. Any foreign substance such as acacia or pectin, however valuable its immediate effect, must either be excreted with more or less rapidity,

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in which case its specific effect is temporary and it serves not at all as a real replacement for the depleted stores of protein and circulating cells, or else it is deposited in the tissues, where it may be positively harmful. Nevertheless, numerous practical considerations force us to be satisfied with substitutes for whole fresh blood, and for many purposes some of these substitutes are so efficacious that the loss is not great. Thus, almost all of us now use refrigerated blood because of its convenience and availability, reserving the use of fresh unstored blood for special conditions.

In the evaluation of blood substitutes the qualities for consideration are first of all effectiveness and safeness. Regardless of all else, our substitute must do its job well without adding unwarranted hazards. Ease and cost of preparation in adequate quantity, simplicity of administration, and capability of storage and transportation are the secondary qualities which determine the choice of a substitute from among those of equal value and innocuousness.

Oxygen transport. Whole human blood is the most effective agent for the transport of oxygen. Blood—fresh, briefly stored, or preserved with added glucose—is the only material available for clinical use which will adequately subserve this function. The older the blood, the fewer are the red blood corpuscles which are intact and the shorter is their expected life in the blood stream of the recipient, although in stored blood there is little change in this direction during the first week. Preservation of blood with added glucose lengthens the life of the cells and retards the increase in fragility, but has the disadvantages of dilution and large bulk. In shock, when inefficiency of the circulation due to lowered plasma volume interferes with the oxygen-carrying power of the blood, the administration of serum, plasma, or any other materials, thereby correcting this condition, at least temporarily, results in improved oxygen transport. All of us have seen patients getting along remarkably well with a red blood cell count of 1,000,000 as a result of gradual blood loss. The plasma volume in such cases will be about normal. In acute severe hemorrhage, however, most patients will not tolerate the loss of even one-half of the total blood volume unless replacement therapy is employed. In other words, although one-half of the red blood corpuscles may still be present in the vascular bed, the patient may yet succumb because of the lowered plasma volume. On the other hand, the early administration of plasma or serum following severe blood loss will render more effective the reduced number of corpuscles remaining and recovery will usually result if the bleeding has been controlled. In such circumstances plasma or serum is not so efficacious as whole blood, but the results are usually satisfactory.

In anemia, then, acute or chronic, whole blood, as fresh as possible, is best. In acute hemorrhage any effective blood substitute may be used while whole blood is being obtained or while hemorrhage is being arrested. To treat a patient with a ruptured ectopic pregnancy or a bleeding gunshot or stab wound with plasma or serum alone is to run unnecessarily the risk of increased hemorrhage due to a rise in blood pressure before bleeding has been arrested. If the hemorrhage can be promptly controlled, this treatment may be safe. It is dangerous to treat vigorous gastric bleeding with plasma or serum unless preparations for operation are under way. Even after the hemorrhage has been controlled the resultant severe anemia will handicap the patient and necessitate blood transfusion. When blood is available it is much better to give it at once. And it can now be made constantly available, in all hospitals at least.

Recently Amberson in Baltimore, Cannan in New York, and O'Shaughnessy in England have aroused interest in the use of hemoglobin alone. Pure crystalline human hemoglobin can be prepared and maintained in stable solution, or lyophilized if desired. Because of the efficiency of extracorpuscular hemoglobin in carrying oxygen, cats can be kept alive 24 to 36 hours on feline hemoglobin after all of their red blood cells have been removed. In addition, this hemoglobin exerts an osmotic effect several times greater than that of the plasma proteins. Human beings have been given large doses of hemoglobin intravenously without ill effect. This employment of hemo-

globin is particularly attractive in view of the volume of red blood cells discarded in the preparation of plasma. The injected hemoglobin, however, soon alters to inactive methemoglobin and in being excreted throws an added burden on the kidneys.

Maintenance of osmotic pressure of the plasma proteins. Shock represents the chief acute condition requiring the reinforcement of this function of the blood. Again, except perhaps in burns, whole blood is superior to all other substances; it treats the shock as effectively and at the same time provides red blood cells and, if fresh enough, white blood cells and platelets as well. The exigencies of medical practice, however, and especially of military medical practice, have been responsible for the search for suitable substitutes.

Both plasma and serum are approximately equally effective. There is a somewhat greater likelihood of unfavorable reactions when serum is employed. Plasma contains fibrinogen, which serum lacks. They are prepared and administered with about equal ease. Plasma is more conveniently employed in connection with blood banks than is serum, but serum is more readily run through bacteriological filters, if that is desired. Both are capable of long storage and transportation—liquid, frozen, or dried. As to the relative merits of the substances in the various physical states, liquid plasma is most readily administered, frozen plasma preserves the various protein elements best, and dried plasma is most conveniently transported. Dried plasma requires expensive and elaborate equipment for large scale production. Liquid plasma offers least resistance to bacterial growth, frozen plasma must be rapidly thawed in a water bath at 37 degrees C., and dried plasma must be regenerated with distilled water suitable for parenteral use. All have the advantage over blood of being capable of long storage and of not requiring matching before administration. In this last respect they are probably safer than blood, although the possibility of bacterial contamination offsets the advantage of freedom from incompatibility reactions. Liquid or frozen plasma seems best suited to civilian use, or to military use on a fixed battlefront, as in England at present. Dried plasma finds its chief employment in shipment to foreign stations and on naval vessels.

Some workers in the field have put forth as an advantage of the dried material the fact that it can be redissolved in a small volume of water, producing a hypertonic solution which, when injected into the blood stream, exerts a powerful osmotic pressure, drawing fluids from the tissues and "reversing the mechanism of shock" as it is stated. Unfortunately most patients in shock—and this is particularly true of soldiers wounded on the field of battle and of burned patients—are not only already dehydrated or in need of fluids, but are entering on a period of their illness when water intake will be of great concern, so that it would be well not to increase the tissue water debt at the start. However, the idea of administering the proteins from a pint of blood in a single 50 cubic centimeter injection is very attractive and offers possibilities for treatment of shock far forward in the battle zone.

It has been found by Dr. Cohn and his associates at Harvard that human plasma can be fractionated into its various protein constituents, which, reduced to pure crystalline states, may be redissolved, forming stable, nonviscid solutions which flow readily through small needles. Albumen, the largest fraction, is the one which exerts the greatest osmotic force. Hypertonic solutions of albumen obtained from alcohol fractionation of human plasma have been employed in a small number of cases and seem extremely effective in the treatment of shock. Unlike the substances which will next be discussed, the albumen thus injected is utilized by the body. Production is said to be cheaper and simpler than the preparation of dried plasma, but quantity production is similarly limited by the difficulties in the procurement of large quantities of human blood. Bovine albumen, prepared by the same method, solves the problems of quantity and cost, but thus far the bovine albumen has not been free from a small fraction of globulin. The occurrence of sensitivity reactions in human beings given this material has been attributed to this fraction. If bovine albumen, which in itself seems not antigenic,

can be obtained in sufficiently pure form to be safe, a very nearly ideal plasma substitute for military use and for some civilian uses will have been found.

Human fluids other than blood and its derivatives have been employed. While pleural fluid, and even that occurring in a case of chylothorax, has been safely injected intravenously, most attention has been paid to ascitic fluid. Of this fluid it may be said that it is similar to plasma, but contains roughly half as much protein and is therefore half as effective for most conditions. It is obtained cheaply but in very limited quantities, and the source of supply is undependable. Experience with it is still small. Earlier workers reported frequent reactions. More recent work, using citrated ascitic fluid, seems to have decreased the incidence of reactions. The fluid can be dried, but it seems a waste of time to start with so dilute a fluid. If it can be shown to be free from danger of reactions, it may form a useful source of additional stores in hospitals.

Attempts have been made to use whole beef plasma. Wangensteen in Minneapolis and Muether in St. Louis have demonstrated that some patients tolerate large masses of bovine plasma intravenously although with frequent sensitivity reactions. During the first World War Brodin and St. Girons employed horse plasma in 500 cubic centimeter quantities in several instances without untoward results. It seems unlikely, however, that whole plasma from other animals can be made safe for human use, although suitable purified protein fractions are a distinct possibility.

Animal protein substances of other origins have been proposed, the latest being gelatin which is derived from fish bladders. Dried fish bladders, sold commercially to brewers, when suitably treated yield a readily soluble powder. Injected into dogs the solution is effective in the treatment of shock, causes no reactions, and is not antigenic. Its use in human beings has not been reported, and here as with other foreign substances we must know that the material is not antigenic and that preferably the protein is utilizable by the human organism and is not treated as a foreign substance to be excreted.

Substances of plant origin have also been investigated. Acacia, the complex carbohydrate derived from the gum of certain shrubs of the genus Acacia, is the chief of these. It was suggested as a blood substitute as far back as 1906 and was first administered to human beings in 1917. It has been proved to be fairly effective in the treatment of shock, but immediate unfavorable reactions have been too frequent and doubt has been thrown on its eventual fate in the body. It is apparently stored in the liver for long periods and impairs the function of the liver in protein formation. It has also been said to combat the treatment of shock by interfering with oxygen absorption by the red blood cells. For these reasons, and because it fails to supply the whole organism with the additional protein usually required in hemorrhage and in traumatic shock, it has not found much favor

More recently, common citrus fruit pectin, commercially supplied for the making of jellies, has been prepared by Hartmann and his coworkers for use as a plasma substitute. Only 8 clinical instances of its use are reported, and in at least 1 a chill occurred. It is apparently nonantigenic in guinea pigs, rabbits, and dogs. In the dog it is largely excreted in the urine in the first 48 to 72 hours. Like acacia it is a foreign material of no demonstrable value to the body after the effect of the initial injection has disappeared.

Least effective of all for the reinforcement either of the oxygen-carrying power of the blood or the osmotic pressure maintenance are the solutions of the crystalloids. Their benefit is purely temporary. In hemorrhage, unless bleeding has been arrested and shock is mild, they may increase blood loss and wash proteins into the tissues as well. We all recall in the recent past, before the ready availability of blood and plasma radically altered the treatment of sudden shock or hemorrhage, the very brief period of benefit from the injection of solutions of glucose or sodium chloride, except in cases of mild shock in which the precipitating factor had been discontinued.

Blood coagulation. The effect on blood coagulation of the various substitutes has not been comparatively studied. Platelets survive in stored blood for 2 to 5 days. Fresh whole

blood or blood refrigerated for a short time probably increases the clotting power of the recipient's blood, and this is probably true of plasma as well. It is not likely that any preparations not derived from human blood will have such power.

Nutrition. In speaking of the nutritive rôle of the blood we are now concerned chiefly with its protein content. While the proteins of the blood are formed elsewhere than in the blood stream, it has been shown that they may be utilized in turn by the body for storage in the tissues. In conditions of chronic hypoprotinemia the administration of whole blood as long as the hemoglobin is low (as it usually is in these conditions), followed by the administration of plasma or serum, is fairly efficacious. Since, as a rule, low plasma proteins are associated with depleted protein stores in the tissues, great quantities of plasma must be administered intravenously before any effect is reflected in the level of the plasma proteins. In conditions of starvation, as in esophageal or gastric obstruction, some improvement may be achieved, but will be maintained only if normal alimentation is restored. In nephrosis and cirrhosis, although alimentation may be unimpaired, the continuing loss of proteins makes the problem more difficult. Amino acids injected intravenously (Elman) have proved their worth in supplying the body with building stones for the formation of tissue and blood proteins when adequate protein cannot be taken by mouth. Whipple and Madden have produced digests of casein by papain which are not split as far as the amino acid stage and which, when administered intravenously, will maintain dogs in positive nitrogen balance indefinitely.

Infection. We can expect only whole blood, plasma, and serum to supply complement and immune bodies. Any blood substitute which supplies utilizable protein will indirectly aid in antibody formation. Human globulin has been purified, as has albumen, and could perhaps find some use in this regard. Substances of plant origin are of no immunological value, and acacia, by interfering with the regeneration of plasma protein in the liver, may be actually harmful.

Phagocytosis. Significant numbers of effective leucocytes can be supplied only by fairly fresh blood. Leucocytes decrease 50 per cent in numbers in 24 hours, and phagocytic activity of those remaining drops after 72 hours, is slight in 5 days, and absent in 7.

SUMMARY

It is obvious that the ideal in replacement therapy is the administration of fluid of the same composition as that which has been lost —whole blood for whole blood and plasma for plasma. The employment of whole blood is rarely contraindicated except in instances of extreme hemoconcentration, such as that which may occur following severe burns. Plasma and serum have the advantage, particularly in emergencies, that compatibility tests are not necessary and delay in treatment can be avoided. Preliminary observations indicate that purified human albumen is a safe and effective substitute for plasma. The problem of providing blood substitutes in large quantities will be greatly simplified if nonantigenic fractions of animal plasma proteins can be prepared.

STAPHYLOCOCCUS SEPTICEMIA

Observations Relative to the State of Hydration in the Dog and in Man

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THE therapeutic problem presented by Staphylococcus septicemia remains a pressing one, in spite of the remarkable advances made in recent years through the development of chemotherapy and the widespread adoption of a physiological approach to therapeusis. The controversy which still exists concerning the efficacy of early or late surgical intervention in acute hematogenous osteomyelitis is characteristic of the confusion in this field and an indication of the fundamental nature of the unsolved problems.

Reports of various investigators stressing the importance of adequate fluid balance in the treatment of burns, intestinal obstruction, and various other acute and chronic surgical diseases, suggested the possibility that fluid imbalance in acute infections may be a factor influencing prognosis. Accordingly, an investigation was initiated having as its object the determination of some of the changes occurring in hydration during Staphylococcus septicemia.

No careful observations on hydration in the toxic phase of staphylococcus infections have been reported. A few fragmentary references indirectly bearing on the matter have been gathered. Webb and Korfmacher concluded that acute infections produce comparatively mild or temporary changes in serum proteins, these changes consisting of a minimal lowering of total protein, a normal or increased globulin and a decreased albumin level. Jones and Eaton in discussing nutritional edema stressed sepsis as one of the important factors in the causation of postoperative edema. Curphey and Orr made the same observation and stated that edema was most frequently associated with starvation accompanying an acute infection such as peritonitis. Shumen and Jeghers in their discussion of the value of routine blood protein determinations listed fever as one of the causative factors of hypoproteinemia.

The importance of adequate fluid balance has been more adequately stressed in the study of other surgical diseases. The present day conception of normal water exchange, particularly as regards its clinical application in surgery, has been emphasized in the work of Coller and Maddock and their associates (4, 5, 6). They have shown that the daily maintenance requirements of fluids for the healthy adult is about 3500 cubic centimeters and that the need may be greater with increased metabolism or abnormal losses of body fluids. This investigation drew attention to the necessity for maintaining an equilibrium of electrolytes in the blood and pointed out the dangers of inadequate or excessive administration of sodium chloride.

Jones and Eaton (11, 12) first called attention to nutritional edema as a problem of clinical surgery. In 1933 they reported observations in 34 surgical patients, having critically low serum protein levels following surgery, in most of whom edema occurred. Subsequently, they showed experimentally that postoperative edema occurred following procedures frequently used in patients. It was their opinion that the production of edema was dependent chiefly upon nitrogen starvation and other forms of malnutrition in association with such factors as excessive intake of water and sodium chloride, profuse surgical drainage, general effects of sepsis, massive hemorrhage, or renal dysfunction. They produced experimental evidence that water can accumulate to a striking degree in any of the parenchymatous organs as well as

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in the subcutaneous tissues and that all of the body functions may be greatly retarded by such an occurrence. Ravdin and his associates showed a definite relation between intestinal and gastric emptying times and the level of plasma protein. They pointed out that the edema of trauma after gastrointestinal anastomosis may be accentuated by a lowered plasma protein level to such an extent that an obstruction due to a technical defect in the anastomosis is mimicked. They further emphasized the effect of hypoproteinemia in decreasing the proliferation of fibroblasts and in producing a tendency to wound disruption after abdominal operations.

Shumen and Jeghers, in recommending study of the plasma proteins as a routine procedure for every patient, pointed out the importance of hyperproteinemia as well as of hypoproteinemia. They called attention to the value of the plasma protein level as an indication of liver reserve and particularly stressed its importance in hyperthyroidism as a means of anticipating and avoiding postoperative crisis. In routine tests on 320 patients they found that edema was present in 23 per cent of the 81 patients whose plasma protein levels fell below 6.00 grams per cent. Kormacher also emphasized the relation of the plasma protein level to the severity of hyperthyroidism and stated that levels of total protein below 6 grams per cent or of albumin below 3 grams per cent are probably indicative of hepatic damage and are reasons for performing thyroidectomy in stages. In his opinion plasma protein estimations offer a definite prognosis in obstructive jaundice, since extensive liver damage is made evident by marked reversal of the albumin-globulin ratio.

The study of the rapid shifts in fluid balance occurring after extensive burns has brought to light the important rôle played by the plasma proteins in these physiological changes. Elkinton, Wolff, and Lee, in a study of 5 cases of severe burns, emphasized the information which is available at the present time. After a 25 per cent burn as much as 53 per cent of the total plasma volume may disappear from the circulating blood within 40 minutes, and the loss continues for as long as 40 hours. During this early period there may be a tremendous concentration of blood. Such fluid imbalance is primarily due to an altered capillary permeability with a shift of fluid and proteins into the tissues, rather than an external loss of these substances. The need for water and electrolytes is moderate only, since the excess fluid in the tissues should be available when plasma osmotic pressure is restored to a normal level. Administration of excessive amounts of normal saline, without plasma protein, only increases an edema already present, and must be given in dangerously large amounts to have any significant effect upon the plasma volume. For the correction of this situation, Elkinton and his associates recommended the frequent intravenous injections of plasma, in amounts varying according to the need, without the administration of excessive amounts of protein free fluids. Scudder (16) recommended the intravenous use of hypertonic saline solution in conjunction with adrenal cortical extract and showed that these agents have a great effect upon plasma volume in the absence of quantitative protein replacement. Throughout the study and treatment of patients with severe burns frequent plasma protein determinations in relation to hematocrit readings are of the utmost value in indicating the proper therapeutic measures.

In 1938, Scudder, Zwemer, and Whipple (18) reported a large series of collected cases of acute intestinal obstruction with an analysis of the clinical and pathological data. Twenty-five patients who came under the direct observation of the authors were subjected to an intensive study. On the basis of these observations the authors drew definite conclusions regarding the efficacy of controlled fluid therapy. The next year, Scudder, Drew, and Sloan (17) reported in detail a case of acute appendicitis complicated by multiple abscesses in which it would appear the patient's life was preserved only because of the direction of treatment by a definite program of fluid control. They emphasized the observation that earlier than blood pressure changes increasing peripheral hemoconcentration foretells impending circulatory collapse, and recommended the adoption of a program of careful fluid balance for all severely ill pa-

tients, stressing the efficacy of concentrated saline, adrenal cortical extract, and plasma as therapeutic agents in combatting impending shock. Scudder and his associates indicated that proper fluid control therapy in surgical conditions producing disturbances in physiological fluid balance can be directed after careful study and rational interpretation of information concerning cell volume and plasma protein levels.

EXPERIMENTAL STUDY

The material presented in this report includes data accumulated from a study of experimental Staphylococcus septicemia in dogs and data acquired in observations of patients admitted on the surgical services of Charity Hospital in New Orleans with diagnoses of Staphylococcus septicemia.

Observations were completed upon 15 dogs divided into two groups of 7 and 8 animals, respectively. Group I was composed of 4 adult dogs and 3 four month old puppies. Group II was composed of a litter of 8 two month old nursing puppies. Throughout the experiments they were given bountiful quantities of pablum and standard dog foods. In addition, Group II puppies were allowed to nurse. Fluids were unrestricted, but no attempt was made to force feeding or to administer treatment.

During 2 weeks preceding the experiments normal values were established for hematocrit or red blood cell count and plasma proteins. Blood cultures were taken repeatedly before the beginning of the experiments and were found to be negative. The method used for plasma protein determination was the falling drop method of Barbour and Hamilton (1, 2, 3).

A strain of hemolytic Staphylococcus aureus recovered from a human case of Staphylococcus septicemia was cultured for 18 hours in dextrose beef heart broth. One cubic centimeter of this inoculum was injected into the right femur of each dog in Group I. Before use in Group II the organism was made more virulent by animal passage, and the 18 hour dextrose beef heart broth culture was concentrated by centrifugation until 1 cubic centimeter of the final inoculum contained 30 x 10^9 bacteria. One cubic centimeter of this preparation was injected into the right tibia of each animal in Group II.

Five dogs of Group I survived, but only 1 animal died as a result of the hemolytic Staphylococcus aureus septicemia. All the animals of Group II succumbed after intervals varying from 2 to 17 days. Determinations of hematocrit or red blood cell count, plasma proteins, and blood cultures, together with clinical observations, were made at regular intervals for 16 days or until the dogs died. Autopsies were performed on the 10 dogs which succumbed. Cultures were taken of the various parts, and sections were prepared for microscopy. Septicemia was produced in all of the animals, but the blood culture colony counts were much higher in the dogs of Group II. Limited osteomyelitis was present in 9 of the autopsied animals. Metastatic abscesses were found three times in the lungs, twice in the liver, and twice in the kidneys. Marked degenerative changes in the liver, kidneys, and heart were constant findings.

In this study of hydration the method employed by Scudder (9, 16, 17, 18) and his associates was used, since the simple determination of cell volume and plasma proteins gives much useful information concerning fluid balance.

It has been shown by Stebbins and Leake that there is a diurnal variation of as much as .0044 in the specific gravity of dog blood. Barbour and Hamilton (3) ascribed changes of .0040 in the specific gravity of dog blood to "emotional anhydremia." Variations are known to occur also in the cell volume and red blood cell counts of normal blood. Because of these normal daily variations in individual animals, composite graphs of the data at hand give more representative pictures of the changes in hydration, occurring in the respective groups of animals under the experimental conditions set forth, than do individual records. Accordingly, observations will be made and conclusions drawn largely on the basis of the composite graphs seen in Figures 1, 2, 3, 4.

Group I. The hematocrit curve (Fig. 1) rose perceptibly in relation to the hyperpyrexia which developed during the first 4 hours after inoculation. Thereafter, there was an uneven

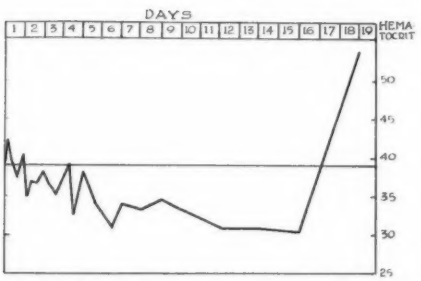

Fig. 1. Group I animals: hematocrit determinations. Average hematocrit curve of 7 dogs during mild Staphylococcus septicemia. The final spectacular rise was caused by a single specimen from 1 animal.

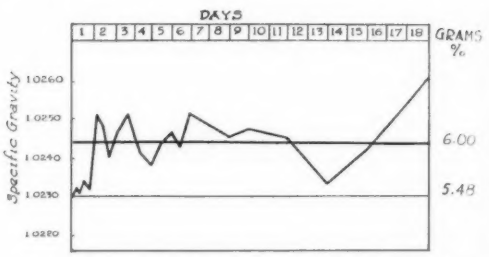

Fig. 2. Group I animals: plasma protein determinations. Average plasma protein curve of 7 dogs during mild Staphylococcus septicemia.

but progressive fall in the average hematocrit level until a value of approximately 30 was reached and maintained for several days. The final spectacular rise in the curve was caused by a single specimen from 1 dog. The average plasma protein curve (Fig. 2), starting from a base line of 5.48 grams per cent, made a considerable rise on the second day after inoculation and maintained itself irregularly at a level well above the base line. The final rise in the curve was formed here also by a single specimen.

By placing the hematocrit and plasma protein curves in relation to each other, one is able to make a reasonable interpretation of the changes which occurred in this particular group of animals. The general picture resembles the "idealized" graph which Drew, Scudder, and Papps (9) thought typical of "water loss with anemia." If it can be assumed that the increased levels of plasma protein were caused by concentration of blood due to water loss, the degree of the anemia was in reality greater than that represented.

Group II. The average red blood cell curve (Fig. 3), beginning at a base line of 3,500,000 cells per cubic millimeter, fell rapidly and consistently to a level of approximately 2,500,000 cells per cubic millimeter which was reached on the sixth day and was maintained thereafter, except for a single specimen from the 1 surviving dehydrated dog on the seventeenth day. The average plasma protein curve (Fig. 4) which rose perceptibly on the second day as did also the curve for Group I, was maintained above the base line only until the fourth day. Thereafter, there was a sharp decline of the curve to a level below 4 grams per cent. The exceedingly low value of 3.16 grams per cent was reached by a single specimen from the 1 dog surviving on the seventeenth day.

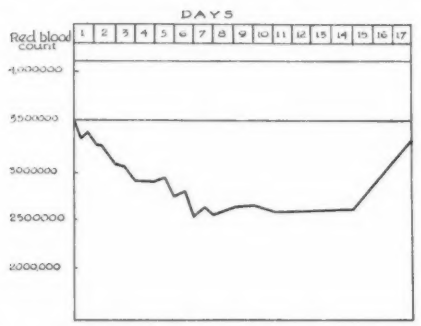

Fig. 3. Group II animals: red blood cell count. Average red blood cell curve of 8 puppies during severe Staphylococcus septicemia. The final spectacular rise indicated a single count from 1 animal shortly before its death.

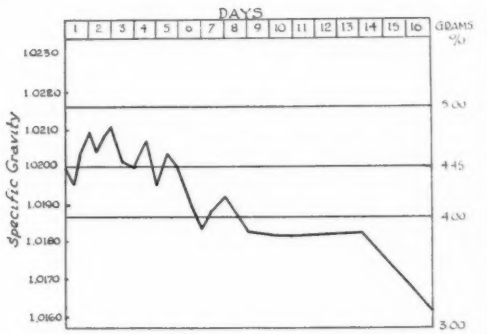

Fig. 4. Group II animals: plasma protein determinations. Average plasma protein curve of 8 puppies during severe Staphylococcus septicemia.

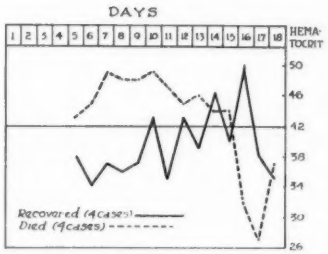

Fig. 5. Clinical Staphylococcus septicemia: hematocrit determinations. Composite graphs of hematocrit determinations during Staphylococcus septicemia in two groups of patients.

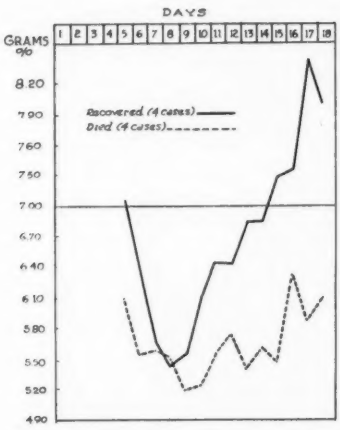

Fig. 6. Clinical Staphylococcus septicemia: plasma protein determinations. Composite graphs of plasma protein determinations during Staphylococcus septicemia in two groups of patients.

Again placing the red blood cell curve and the plasma protein curve in relation to each other, one is enabled to make a reasonable interpretation of the variations in fluid balance which occurred. During the first 4 days following inoculation, when there was a steady fall in the hematocrit curve but a moderate increase in plasma protein values, the relation resembled the idealized "water loss with anemia" picture seen in Group I. Between the fourth and fifth days the relation of the respective curves changed to one indicating both red blood cell and plasma protein depletion. If clinical judgment to the effect that the animals were in states of comparative dehydration is correct, the true values for red blood cells and plasma proteins were even lower than those indicated by the curves.

Reasons for the marked decline in the hematocrit curve and the red blood cell curve in the respective groups of animals remain matters for speculation. The actual blood loss incident to the frequent taking of specimens was not great. Since less than 20 cubic centimeters of blood was withdrawn from any animal of Group II in the 25 days during which the observations were made, it does not seem probable that blood so lost figured largely in the more than 28 per cent decline in the red blood cell level. The possibility that there was a depression of the hemopoietic function of the bone marrow is not borne out by the marked erythroid and myeloid activity seen in sections of the bone marrow. Malnutrition may have been a factor, although in each group the greatest decline in the curves occurred by the sixth day after inoculation, which is a relatively short period for changes from malnutrition to become evident. Staphylococcus hemolysins are capable of rapid destruction of blood; however, microscopy did not reveal any unusual amount of pigment in the reticuloendothelial system, nor was jaundice seen clinically. Loss of hemorrhagic exudates into the intestine and lungs and by external discharges may have been a causative factor in the anemia of 2 of the dogs.

It is easier to suggest reasons for the variance of the plasma protein curves of the two groups, inasmuch as differences in the respective clinical courses were marked. The matter of exudates supplies a ready explanation. Whereas 5 of the animals of Group II produced copious exudates, only 1 dog in Group I lost any considerable amount. However, 2 dogs, which had no marked exudative loss, had lower protein levels than the other animals in Group II.

Destruction of plasma proteins by the direct action of a staphylococcus toxin must remain a hypothetical possibility. Indirect action of such toxins in causing degenerative changes in the liver offers a more likely explanation, if it can be assumed that the advanced state of cloudy swelling and fatty degeneration, observed in all of the histological

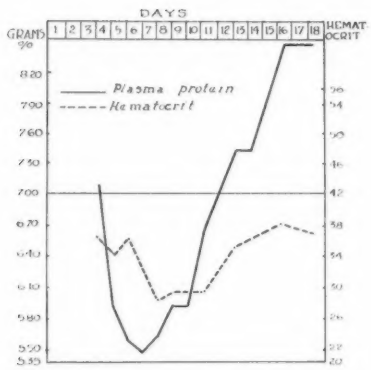

Fig. 7. Graphs of hematocrit and plasma protein determinations during Staphylococcus septicemia in a boy of 12 who recovered. This patient received 1975 cubic centimeters of blood by transfusion between the fourth and eighteenth days.

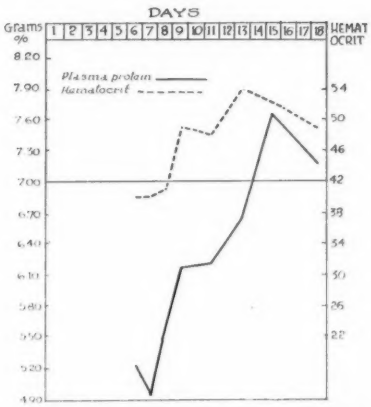

Fig. 8. Graphs of hematocrit and plasma protein determinations during Staphylococcus septicemia in a girl of 13 who recovered. This patient received 3250 cubic centimeters of blood by transfusion between the sixth and thirteenth days.

sections of liver, was due, in part, to bacterial toxins. Since the liver is thought to assume an important rôle in the production of proteins, the level of the plasma proteins may be an important indicator of liver health. The relation between hypoproteinemia and liver damage in hyperthyroidism and obstructive jaundice has already been mentioned (14). Attention has been directed, also, to hepatic changes reported after experimental dehydration (8). Animals in Group II became more dehydrated than those of Group I, and it is probable, in view of the procedure used and the clinical course followed by each group, that dogs of Group II were exposed, also, to bacterial toxins of greater potency and in greater amounts. It is reasonable to suppose that the degenerative changes observed in sections of liver removed at autopsy were greater than those in the animals which survived, and that a lower plasma protein level occurred in Group II partly as a result of more extensive liver degeneration.

Failure to find edema in the face of extremely low plasma protein levels is one of the interesting observations of the study. In 5 animals of Group II plasma protein determinations of less than 3.7 grams per cent were recorded. Jones and Eaton (11), in reporting repeated estimations of less than 3.6 grams per cent in a patient, never subject to edema, suggested that the explanation lay in the exaggerated state of dehydration of their patient. Curphey and Orr and Keefer stated that edema rarely occurs, even in the presence of very low plasma protein, without the administration of the sodium ion, usually as sodium chloride. Explanation of the absence of edema in these experimental animals may be found, therefore, in their dehydration and their failure to receive any considerable amount of sodium chloride.

CLINICAL STUDY

Sixteen Charity Hospital patients, each having a clinical diagnosis of Staphylococcus septicemia, were observed, and, of these, 8 were chosen for this report. Repeated blood cultures drawn from each of the 8 patients were positive for the hemolytic Staphylococcus aureus. Controlled fluid therapy was employed in each instance, but varied in detail according to the training and diligence of the respective internes and residents. Frequent hematocrit and plasma protein determinations were made in order to furnish data for comparison with those obtained in the study of the experimental animals. Four of the patients survived, whereas the remainder succumbed. In order to correlate the findings in this study with those obtained in the experimental investigation already described, the 8

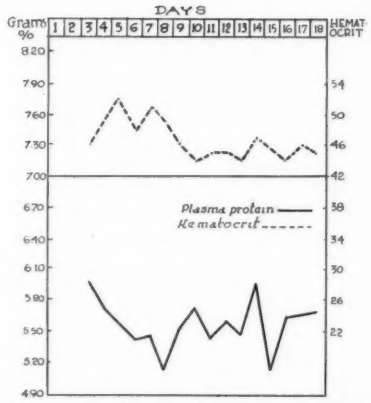

Fig. 9. Graphs of hematocrit and plasma protein determinations during Staphylococcus septicemia in a young adult male who died. Blood transfusions were small and comparatively infrequent, 2760 cubic centimeters being given between the third and eighteenth days.

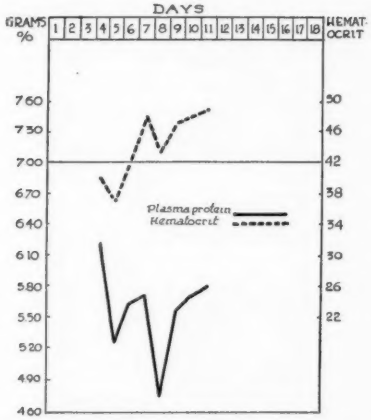

Fig. 10. Graphs of hematocrit and plasma protein determinations during Staphylococcus septicemia in a girl of 14 who died in spite of comparatively large amounts of blood by transfusion (3900 cubic centimeters between the fourth and eleventh days). This patient was one who became markedly edematous before death.

patients were divided into groups according to survival. Compositve graphs of each group's hematocrit and plasma protein readings were made.

Figure 5 shows the composite graph of the hematocrit determinations in each group of patients. It fails to demonstrate the consistent lowering of the hematocrit level which was so striking in both Group I and Group II animals of the experimental study. It would appear that the numerous transfusions which these patients received were sufficient to maintain or raise to comparatively normal levels the hematocrit in those patients who succumbed as well as in those who recovered. Figure 6 shows the composite graph of the plasma protein determinations in each group of patients. Here a striking difference is observed in the response of the two groups. Each curve fell sharply immediately after admission of the patients to the hospital as adequate hydration was obtained by the employment of parenteral fluids. In the course of treatment, however, the plasma protein curve of those patients who survived rose rapidly to normal and even unusually high levels; whereas, the composite curve of those patients who succumbed failed to show this response. These later observations correspond to those in the experimental study in which it was observed that the plasma protein curve of the Group I dogs which survived maintained a better than average height, whereas, the curve of the Group II dogs which succumbed fell consistently.

Corroboration of the impressions conveyed by the composite graphs may be had by an examination of Figures 7, 8, 9, and 10, which show the hematocrit and plasma protein curves of each of 4 patients. Graphs of patients who survived are shown in Figures 7 and 8. Comparatively large amounts of citrated blood were given to each child, and the plasma protein response was striking. Graphs of patients who succumbed are found in Figures 9 and 10. In each instance the hematocrit curves were maintained at a high level by the frequent transfusions, but there was no like response on the part of the plasma protein which remained at subnormal levels until the death of each patient. The patient whose graphs are shown in Figure 9 was an adult male, who, undoubtedly, received transfusions of blood too infrequently and in too small quantity. It is a matter of speculation whether or not larger and more frequent transfusions might have raised the plasma protein level to normal, thus influencing favorably the ultimate outcome. The patient represented by Figure 10 died in spite of comparatively large

and frequent transfusions and her plasma protein level, though rising, had never reached a normal point. It is interesting to note that 2 of the patients became quite edematous before death; in each instance this followed the injudicious use of sodium chloride administered intravenously.

CONCLUSIONS

Although the number of experimental animals and of patients observed during this study is comparatively small, the data accumulated have been so consistent in certain respects that they were deemed worthy of report, particularly since there seems to be a justifiable practical application.

In experimental Staphylococcus septicemia in dogs there was a marked fall in the hematocrit level both in animals fatally ill and in those ultimately recovering. Patients afflicted with Staphylococcus septicemia, whether they survived or died, were able to maintain normal hematocrit ranges with the aid of numerous transfusions.

In untreated experimental animals and in patients undergoing intensive therapy a distinct line is drawn by plasma protein levels between those (animals and patients) who survived and those who succumbed. The plasma protein curves of the former maintained or reached a better than average level, whereas the curves of those who succumbed steadily fell or failed to rise even in the instance of the patients who received intensive treatment including numerous blood transfusions.

It is our belief that these observations are a sufficient basis for considering the plasma protein levels observed clinically in Staphylococcus septicemia as a valuable prognostic aid. It would appear that the plasma protein level falls in all patients having Staphylococcus septicemia, but that in those instances in which recovery is to occur, the proteins rise and are maintained at a high point after adequate therapy. Since it has been shown that the plasma protein responds more slowly to repeated transfusions than does the hematocrit, the former should be used as a therapeutic guide to indicate the need for blood transfusions. Large amounts of whole blood or plasma, repeatedly administered, give the greatest opportunity for recovery.

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CHEMOTHERAPY AND ROENTGEN RADIATION IN CLOSTRIDIUM WELCHII INFECTIONS

Clinical and Experimental Studies

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CLINICAL clostridium infections range in severity from relatively benign infections to more fulminating and malignant types. The etiological organism may be either Clostridium welchii, Clostridium septique, or Clostridium oedematiens, or a combination of the three. Our present clinical and experimental studies are confined to Clostridium welchii, for this is by far the most common offender clinically.

There is doubt in the minds of many as to just what "gas gangrene" really is. The present controversy over the proper therapeutic measures leaves no doubt that many criteria may be loosely interpreted. The term "gas cellulitis" or "clostridium cellulitis" is suggested not to supplant the term "gas gangrene," but to provide a hitherto missing category in which to place the milder, the borderline, and the atypical case.

We have come to give less credence to the term "gas gangrene." Does such an entity really exist, or does it simply include the more fulminant cases of clostridium cellulitis? "Cellulitis," either used or implied, is a more inclusive term and is perhaps more apt in emphasizing the bacterial origin and nature of the infection. There are cases that have become fulminating within several hours, and there are other cases which have developed slowly. The infection may extend largely in the subcutaneous tissues in one patient, or in both the subcutaneous tissue and muscle in another, even though both patients are equally sick. There have been a few cases of superficial Clostridium welchii infection with persistently positive cultures, at times with small amounts of gas in the immediate vicinity but with an essentially benign course. These latter cases have been excluded from the present series even though we believe that they are milder manifestations of the same infection.

It is possible that the disease which we are accustomed to see differs in some way from the classical description. Definite muscle involvement is usually not proved now that more conservative measures are used. In our study, therefore, the criteria for calling cases "gas gangrene" are: (1) positive cultures of Clostridium welchii; (2) spreading infection; (3) gas in the tissues; and (4) discoloration and edema of the involved structures (17).

One of our first concerns has been to establish the presence of a true "gas gangrene." Regardless of whether or not this is done, any spreading infection with Clostridium welchii found in the culture, or any infection with gas in the tissues has been treated as a severe case. If the four criteria were not all met, the case was not included in our series. Among those omitted were 4 simple Clostridium welchii infections, 2 of which presented small amounts of gas in the tissues (Table I). In 2 additional cases, crepitus was noted but no Clostridium welchii were found. The offenders were Escherichia coli in one case, and in the other an anaerobic streptococcus and a hemolytic staphylococcus.

CLINICAL EVALUATION OF PRESENT THERAPEUTIC AGENTS

Sulfanilamide, sulfapyridine, sulfathiazole, roentgen irradiation, antisera, zinc peroxide

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TABLE I.—CLINICAL WOUND INFECTION WITH CLOSTRIDIUM WELCHII

Name	Age	Cause	Treatment	Result
W.R.	27 yrs.	Mangled fingers	Sulfanilamide, irradiation	Well
J.W.	35 yrs.	Mangled fingers	Irradiation	Well
P.W.	2 wks.	Infected heel	Irradiation	Well
G.R.	38 yrs.	Cirrhosis of liver, thigh abscess	Sulfadiazine, irradiation	Died (wound clean)

pastes, and the inhalation of high concentrations of oxygen have each been recommended recently for the treatment of Clostridium welchii infections. The multiplicity of these agents and the disparagement which each in turn has received implies that a method of appreciable superiority is still wanting. On the other hand, the mere fact that no one is advocating a continuation of the previously prevalent radical surgery suggests that the various sulfonamide drugs, roentgen irradiation, or the antiserum may each favorably modify the course of the disease. We believe that the diversity of opinion regarding the relative merits of any one of these therapeutic agents may in part be due to the wide variation in the severity of this type of clinical infection: that is, a true "gas gangrene" as here defined, or a "clostridium cellulitis."

Antiserum. The polyvalent antiserum, inefficient at best when used alone, can easily be proved to be of some value experimentally (10, 13). In mice and guinea pigs it is more efficacious than is sulfanilamide. In clinical use, the polyvalent antiserum gives acceptable results when used with conservative surgery, but prophylactically its effect is feeble (1, 14). That this should be so follows rationally when one compares the antiserum for clostridium infections with the antiserum for tetanus. In the latter disease the antiserum combats, and very effectively, the tetanus exotoxin which has a systemic effect, while the action against the usually insignificant local lesion is minimal. The local source of infection is usually small and tends to heal itself.

In the case of Clostridium welchii infections, the antiserum may well control the exotoxins distributed throughout the body, but these are of far less magnitude than is the virulent local lesion which progresses rapidly, killing more tissue and forming exotoxins far in excess of the amount that the polyvalent antiserum can control.

In prophylactic use, the same situation holds. The tetanus antiserum neutralizes the exotoxins as they are liberated from the small local wound. In Clostridium welchii infections, the local lesion tends to spread, often rapidly, regardless of the systemic effect of the exotoxin. Therefore, the welchii antiserum could act through its effect on the local lesion immediately adjacent to the wound. At best it could only slow down the advancing necrosis.

For these reasons we do not insist on the use of Clostridium welchii antiserum either prophylactically or therapeutically. We have used it but twice in our last 18 cases. It is important to note, however, that the protective action of the antiserum in small animal experiments is far greater than it is in humans.

Surgery. In contrast to the past, the need for amputation now is dictated not as much by the infection as it is by the state of the vascular bed. The coexistence of vascular damage to an extremity plus a Clostridium welchii infection has often distorted the picture. The infection was held mainly to be responsible for not only the gas, edema, and seropurulent exudate, but also for the massive necrosis, discoloration, and particularly malignant course. While the radical measure of amputation is still accepted in this extreme, there is no question but that a wound infection with only Clostridium welchii or with other contaminants, too, may run an exceedingly indolent course. When in the muscle (deeper wounds), the progression is more rapid and more serious and there is evidently a distinct local necrotizing effect of the toxin. However, this is shared by other organisms and is seen not infrequently. Perhaps the most common of the others is the cellulitis caused by the streptococcus. The opportunity for growth of Clostridium welchii not shared by the other organisms is the remarkable ability to form gas. This may facilitate the dissection along fascial planes and cause a certain amount of pressure to be exerted.

The contrast between the classical picture of a gas gangrene and many of the wounds

TABLE II.—TRUE CLINICAL GAS GANGRENE (MORTALITY 33.3 PER CENT)

Name	Age	Cause	Treatment	Result
K.S.	44	Compound fracture, amputation	Irradiation, antiserum, sulfanilamide	Slow recovery
T.W.	85	Arteriosclerotic gangrene, amputation	Irradiation, sulfanilamide	Dead
W.D.	70	Diabetic gangrene, amputation	Irradiation, sulfanilamide	Dead
C.M.	46	Compound fracture, débridement	Irradiation	Living
M.J.	68	Arteriosclerotic gangrene	Minimal sulfanilamide, irradiation	Dead
F.K.	62	Arteriosclerotic gangrene, amputation	Irradiation	Slow recovery
C.N.	9	Surgical scarlet fever of arm	Irradiation, sulfanilamide	Well
J.M.	46	Abscess of leg	Sulfadiazine	Well
J.W.	18	Compound fracture of forearm	Irradiation, sulfadiazine	Well

TABLE III.—CLOSTRIDIUM WELCHII INFECTION OF ABDOMINAL WALL WITH TISSUE NECROSIS OF GREAT EXTENT

Name	Age	Cause	Treatment	Result
J.M.	50	Perirectal abscess, diabetes	Irradiation, antiserum, sulfanilamide, drainage	Living
J.M.	72	Extravasation of urine, syphilis	Irradiation, sulfathiazole, drainage	Living
A.M.	62	Ruptured appendix	Irradiation, sulfanilamide, drainage	Living
S.M.	72	Strangulated hernia	Irradiation, sulfanilamide, drainage	Living
C.T.	32	Intestinal obstruction, enterostomy	Irradiation, sulfanilamide	Died 3 days
J.H.	17	Carcinoma of testicle	Irradiation, sulfanilamide	Died 30 days after treatment

seen in civil life suggests that there are many of these infections which might be called "clostridium cellulitis" or "gas cellulitis." Many of the latter are quite fulminant, and easily fulfill the criteria of a "gas gangrene." However, the presence of a relatively intact vascular bed leads to conservative measures.

In arteriosclerotic gangrene and in similar infections, amputation is going to be necessary in a number of cases regardless of whether a Clostridium welchii infection is present or not. Therefore, it is too much to presume that any measure will cure the infection at a site where the part is unable to survive even without the infection. The appearance of the disease in a stump following amputation may well be treated conservatively by simple drainage measures plus one of the sulfonamides or roentgen irradiation, rather than by higher amputation. This is assuming that a relatively intact vascular bed is present in the stump.

In the traumatic cases in which there is considerable destruction and mangling of the tissues (and again assuming that there is no great arterial damage), the infections may safely be treated conservatively. With adequate drainage (we do not use débridement although many advocate it) and the use of roentgen irradiation or a sulfonamide, we believe that we have obtained good results.

Roentgen irradiation. In this series we have included every patient who has been in the Strong Memorial Hospital with "gas gangrene" since 1937 (Tables II and III).

Roentgen irradiation has a definite beneficial effect on the course of the disease. During the last 4 years we have seen fit to use this agent in all but 1 of our cases. In several instances the response to irradiation has been clearcut since no other therapeutic measures were being taken at the time (17).

On the other hand, our results with roentgen irradiation have not been as good as have those of Kelly (11). There have been 5 deaths in our series of 15 cases of "gas gangrene." One of these (C.T., Table III) was a frank therapeutic failure. Another death occurred 30 days after the infection had been controlled and treatment had been stopped. Since death was caused by an advanced carcinoma of the testicle, perhaps this case should not be included as a failure.

The remaining 3 deaths occurred with considerable similarity in patients 68, 70, and 85 years old in whom the general physical condition was poor (Table II). The Clostridium welchii infection did not seem to have any more bearing on their demise than did coexistent pneumonia and advanced arteriosclerosis. Two of these 3 patients had recently suffered amputations because of arteriosclerotic vascular disease of the legs. On the other hand, there have been several reports of distinctly unfavorable outcomes (6, 7). Caldwell's studies of the effect of irradiation on guinea pigs led him to believe that irradiation

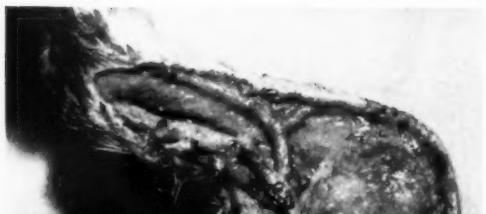

Fig. 1. Photograph of control dog 10 days after inoculation.

Fig. 2. Photograph of dog treated with sulfadiazine 10 days after inoculation.

was of extremely little value (5). More recently a series of studies of compound fractures contaminated by Clostridium welchii were reported (4). In that series, all of his control animals died while 30 per cent of the treated animals survived.

Sulfonamides plus roentgen irradiation. Is the use of both irradiation and a sulfonamide advisable? Until recently there has been no clinical or experimental proof that these two should not be used together. It has been suggested that the combined use is contraindicated (11, 12). Until the last few months we had assumed, perhaps unjustifiably, that the measures were probably complementary. The majority of our patients were given either roentgen irradiation plus sulfanilamide, or roentgen irradiation plus sulfadiazine with success. As we see only 3 or 4 clinical cases of Clostridium welchii infection a year, it is impossible to present a series of any significant size. However, if we assume that our method of approach in dogs is reasonably comparable, roentgen irradiation plus sulfadiazine gives poorer results than does either one alone (Table IV).

Sulfonamides. Although the use of the sulfonamide drugs is in favor, only a few small series have appeared (2, 17). These have been treated mainly with sulfanilamide. Our experience is not conclusive since most of our patients have been treated predominantly by irradiation, and more recently by sulfadiazine. Sulfanilamide was used in 10 earlier cases because we believed that it might prove to be an adjunct to roentgen irradiation. In the few instances in which the patient was maintained on the drug alone for a reasonable period before irradiation was started, the infection was not brought under control.

These scattered clinical impressions are borne out fairly accurately by the experimental results. Four observers (3, 4, 9, 10) have found that in guinea pigs there is a distinct protective action and some curative effect by the drug. Others disagree, but admit that sulfathiazole has some effect (15). Sulfathiazole is more efficacious than either sulfanilamide or sulfapyridine (10, 15) and again the best experimental results were obtained by local use. No reported series is yet available, but Wilson mentions that sulfathiazole plus antiserum and conservative surgery are being used predominantly on these infections in England at present. One patient that we treated with both sulfathiazole and roentgen irradiation made a satisfactory recovery.

We have given sulfadiazine to 3 patients with Clostridium welchii infections in addition to applying it to the local lesion. In each case the infection was brought under control rapidly, and within 2 to 3 days clean granulations covered a good portion of the affected area. One of these patients received nothing at any time but sulfadiazine, while in the other 2, this was supplemented by roentgen

irradiation. One of the latter died from other causes.

EXPERIMENTAL CLOSTRIDIUM WELCHII INFECTION IN DOGS

Roentgen irradiation in clostridium welchii infections was used for about 6 years before there was any experimental confirmation of its action. In large part this was due not to a lack of effort, but to a lack of adequate proof. Our first year of laboratory investigation was conducted on guinea pigs. We were not able to produce a satisfactory facsimile of a human "gas gangrene" because the spread through the tissues was so rapid that it became a generalized disease rather than a local one so that local roentgen irradiation was not effective. The irradiated group did a little better than the controls but the results were not statistically significant.

For an experimental test of the effects of roentgen irradiation and chemotherapy, we have produced Clostridium welchii infection experimentally in 255 dogs. This results in an infection which is quite similar to the disease in humans and is one which progresses somewhat more slowly through the tissues than it does in smaller animals (8).

The disease was produced by injecting 1.2 to 1.5 cubic centimeters of a 20 hour, deep meat, subculture of a single strain deep into the thigh muscles. This strain was from a fatal case of Clostridium welchii infection and had remained undisturbed in an icebox for 6 months. By taking the subculture each week from this master culture we were able to minimize the changes in toxicity and virulence that one working with these preparations must contend with.

Usually within 3 hours after injection, there was edema and tenderness of the thigh with gas palpable deep in the tissues. When undisturbed, the infection progressed rapidly. It dissected into the lower thigh and up into the abdominal wall usually with a fatal result in 24 hours.

Roentgen irradiation. Of the 89 animals in the irradiation group, 50 received roentgen irradiation after the infection had become established (therapeutic irradiation), and 39 were kept for controls. The experiment was carried out in groups of 4 to 10 dogs injected simultaneously. Of the irradiated animals, 26 per cent survived (Table IV), and of the control group, 17.9 per cent survived. From the experimental standpoint, roentgen irradiation would not seem to be logical as a prophylactic measure.[1]

TABLE IV.—COMPARISON OF SULFADIAZINE, IRRADIATION, AND COMBINATION OF TWO USED THERAPEUTICALLY IN DOGS WITH CLOSTRIDIUM WELCHII INFECTION

	No.	Survivals	Per cent
Roentgen irradiation	50	13	26
Controls	39	7	17.9
Sulfadiazine	25	7	28
Controls	15	1	6.7
Sulfadiazine plus roentgen irradiation	25	3	12
Controls	12	3	25

Sulfadiazine and roentgen irradiation. When sulfadiazine combined with roentgen irradiation was given after the infection was well established in 25 dogs, there was a survival of only 12 per cent (Table IV). We have no explanation for this apparently antagonistic effect between roentgen irradiation and sulfadiazine. Work in progress may clear up this paradox. For the present we offer it only as preliminary evidence that the two methods are not complementary and should not be used in conjunction with each other.

Sulfonamides. Our experience with sulfanilamide in dogs is comparable to that of other workers in this field. When used *prophylactically* (if the concentration of the drug in the blood is raised to therapeutic levels prior to the inoculation with the infectious agent), sulfanilamide gave a survival of 60 per cent in 15 dogs. Under the same conditions, butyryl sulfanilamide (a highly soluble preparation of sulfanilamide) gave 30 per cent survival out of a group of 10 dogs, while of 37 dogs in the control group, there was only a 16 per cent survival (Table V). When sulfanilamide is used *after* the infection is established, the advantage over the control group should be considerably less as judged by our results with

[1]The same group of controls has frequently been used for one or more experiments run concurrently.

TABLE V.—CLOSTRIDIUM WELCHII INFECTION IN DOGS TREATED PROPHYLACTICALLY

	No.	Survivals	Per cent
Controls	37	6	16
Butyryl sulfanilamide	10	3	30
Sulfanilamide	15	9	60
Sulfadiazine	25	22	88

TABLE VI.—SULFADIAZINE TREATMENT OF DOGS AFTER CLOSTRIDIUM WELCHII IS ESTABLISHED

	Dogs	Survivals	Per cent
Sulfadiazine	25	7	28
Control	5	1	6.7

sulfadiazine. Other variations of the technique suggest that the drug used locally is a little more efficacious than when given parenterally. In view of the results obtained with sulfadiazine, the prophylactic value of these two drugs was not sufficient to warrant a therapeutic test on dogs.

These results are fairly consistent with the reports of others for Clostridium welchii infection, but with Clostridium septique and Clostridium oedematiens there is considerable contradiction (9, 10, 16).

Sulfadiazine. Sulfadiazine has been superior in our hands to other drugs. When used *prophylactically*, in 25 dogs with experimental Clostridium welchii infection, there was an 88 per cent survival. The control group of 37 dogs (the same used in the preceding group) presented a 16 per cent survival. As shown in Table V, this is appreciably better than any results we had obtained with sulfanilamide preparations. After the infection was established in 25 dogs, the sulfadiazine was given therapeutically (3 hours after inoculation), and there was still a 28 per cent survival. This is in contrast to a survival of 6.7 per cent of 15 control dogs run concurrently (Table VI). None of the procedures used has actually aborted the infection.

In the prophylactic experiments with sulfadiazine, many of the animals showed none of the toxic symptoms which we were accustomed to see. The dogs would often feel well enough to walk about instead of lying prone in their cages. The accompanying photographs (Figs. 1 and 2) show the difference between a control and one of the sulfadiazine treated dogs at the end of 10 days.

CONCLUSIONS

From our experience it seems that a number of cases of Clostridium welchii infection fall awkwardly into the group called "gas gangrene." For this group the term "clostridium infection" seems rather inadequate, but "clostridium cellulitis" is a reasonably descriptive term. There is undoubtedly a wide variation in the manifestations of the disease.

The complementary use of conservative surgery with either a sulfonamide or roentgen irradiation gives as good results as we know how to obtain at present. The reservation of amputation for these cases in which there is a markedly compromised vascular bed is warranted.

Both sulfanilamide and roentgen irradiation when employed alone have some beneficial effect on the course of the infection both experimentally and clinically, and lately we have used sulfadiazine in 3 patients with success. All of these observations are borne out more or less clearly by animal experimentation. The results have been especially encouraging with sulfadiazine. The prophylactic use of the sulfonamides is invariably superior to administration of the drug after the infection is under way.

The development of the experimental aspects of the studies has been delayed by the variance of strains, loss of virulence, and by the multiplicity of therapeutic measures used. All of these variables must be considered in grading experimental results.

We believe that it is essential, particularly in the study of this infection, to reproduce a disease which resembles closely that seen in humans. In our hands this ideal has been more nearly fulfilled in dogs than with any of the other laboratory animals. The resemblance is closer to the human reaction in all respects. As seen from the charts, there are always a few of the controls that survive (6.7 to 25 per cent),[1] but there has always been a

[1] Of 53 consecutive control dogs, the average survival has been 16.9 per cent.

distinct contrast between them and the treated animals. Out of the 255 dogs used to date, only 1 has not developed the disease. This was the only animal not included in the results. This 1 animal had a high antiwelchii titer in the blood, and we assume that he had had a previous exposure to the organism. There is a relative immunity developed in these animals after 1 inoculation with Welch's bacillus (8).

From the experimental standpoint it should be emphasized that we are dealing here with a "pure" infection uncontaminated with secondary invaders. This work in no way invalidates the clinical reports of others who are to be admired for their tenacity in pioneering in the treatment of this disease clinically (11, 12). We have presented experimental data in dogs showing that roentgen irradiation is a valuable asset in the absence of a specific which is still to be found. At the present time, the simplest therapeutic attack seems to be chemotherapeutic in nature (sulfadiazine or some allied compound).

SUMMARY

1. Many of the virulent infections caused by Clostridium welchii are more of the nature of a cellulitis than a gas gangrene.

2. Radical surgery is recommended only in cases of severe vascular damage.

3. Sulfanilamide or roentgen irradiation, when used alone, exerts a beneficial influence on the course of the disease, and to about the same degree. Sulfathiazole is probably somewhat more efficacious. Sulfadiazine is superior to any other drug or method of treatment (experimental proof only).

4. The combined use of both sulfadiazine and roentgen irradiation has given poorer results experimentally than has the use of either separately.

5. The Clostridium welchii antiserum is of some efficacy only when additional methods are used to combat the local lesion.

6. Conservative surgery coupled either with a sulfonamide or with roentgen irradiation is the treatment of choice. At present we recommend conservative surgery plus sulfadiazine.

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THE VALUE OF SULFATHIAZOLE IN THE TREATMENT OF PERITONITIS AND ABSCESSES OF APPENDICAL ORIGIN

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IN a previously reported series (1) of 479 consecutive cases of peritonitis or abscess of appendical origin, in all of which the condition was treated at the Johns Hopkins Hospital by immediate operation, there were 48 deaths, a mortality rate of 10 per cent. This mortality rate compares favorably with those reported from other hospitals of similar size and is somewhat lower than the average of results reported for the delayed or expectant treatment of perforative appendicitis. A study of the fatal cases, however, showed that at least 14 of the deaths were the result of inadequate diagnosis and treatment of complications which arose days or weeks after the initial operation.

Since then 2 years have elapsed, during which period a second group of consecutive cases has been treated. This series although numerically smaller, resembles the earlier one exactly as regards type of patients, proportion of appendical perforations on admission, and incidence of the various postoperative complications, but less than half of the expected number of deaths occurred. The treatment of the patients in this second group differed from that of the earlier series by the use of sulfathiazole in nearly all instances, and by more careful observation and treatment of those patients who did not recover promptly after operation. As in the earlier series, every patient was subjected to immediate operation. From September 1, 1939, to September 1, 1941, there were 105 patients who had peritonitis or abscess of appendical origin, and only 5 of them died. Postmortem examination was made in 4 of these.

Others have reported on the use of sulfanilamide and related drugs in the treatment of perforative appendicitis, and in most instances the drugs have been used locally in the wound, or in the peritoneal cavity. In the present series of cases sulfathiazole was administered intravenously and/or by mouth, none being used locally. It was desirable to give this method a thorough trial so that an evaluation could be made, and it seemed that spreading infections, and infections of extra-appendical origin, such as pneumonia, might be more effectively dealt with in this manner. An initial dose of 4 grams of sulfathiazole was given to the average adult, and this was followed at regular intervals by a sufficient amount of the drug to maintain a level in the blood of 6 to 8 milligrams per cent. The first dose or two was usually administered intravenously, and thereafter the drug was given by mouth unless it was found that the patient was unable to retain it.

TABLE I.—GENERAL SUMMARY OF RESULTS

	No. patients	No. deaths	Per cent
Appendicitis with perforation and abscess	42	1	2.38
Appendicitis with perforation and peritonitis	63	4	6.35
Totals	105	5	4.76

TABLE II.—CHIEF CAUSES OF DEATH

Cause of death	No. deaths From 1931–1939 (In 479 consecutive patients)	No. deaths From 1939–1941 (In 105 consecutive patients)
Direct complication of appendicitis		
Generalized peritonitis	13	2
Pylephlebitis	4	0
Septicemia	1	0
Mechanical ileus	7	0
Subphrenic abscess	5	0
Rectovesical fistula	1	0
Spontaneous rupture of untreated pelvic abscess	1	1
Extra-appendical complications		
Cerebral accident	1	0
Pulmonary embolism	3	1
Pneumonia	4	0
"Poor-risk" patients	4	1
Cause of death uncertain	4	0
Total	48	5

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Anyone familiar with the use of sulfathiazole is aware of the various manifestations of drug intoxication. These include fever, rash, and conjunctivitis chiefly; nausea and blood destruction do not occur so frequently. All of these phenomena were observed in the present series, and on a few occasions it was necessary to discontinue the drug, but this happened in only 1 of the 5 fatal cases.

Table II offers an interesting comparison. Despite the smaller size of the second group certain remarks may be made. I believe that the low incidence of deaths from generalized peritonitis is due to the effect of sulfathiazole, and in the cases of the 2 patients who succumbed the postoperative course was prolonged far beyond the most optimistic expectations.

The absence of deaths resulting from unrecognized mechanical ileus or from unrecognized subphrenic abscess is not due to the lack of these complications, for they occurred with their usual frequency, nor can the fact be ascribed solely to the use of sulfathiazole. It is in this group of patients, with complications treated inadequately in the earlier series, that better methods of postoperative care have brought about improved results.

The single patient considered to be inadequately treated was a 7 year old boy who had generalized peritonitis of appendical origin. He improved steadily for 8 days after operation, and then a definite pelvic abscess formed. This was recognized, but palliative therapy was attempted rather than surgical drainage. On the thirteenth day after operation the abscess suddenly ruptured, and the patient died in a few hours.

That no deaths occurred from pneumonia is probably the result of the chemotherapy.

The single fatality placed in the "poor risk" category was that of a male of 58 years who entered the hospital with generalized peritonitis and in acidotic coma. He was found to have diabetes mellitus, and the blood contained 460 milligrams per cent of sugar. Efforts to regulate the diabetes and to improve his condition generally were unavailing. He died 2 days after operation.

In summary, it can be fairly stated that sulfathiazole given by vein or by mouth is a useful adjunct to the treatment of perforative appendicitis. An equally potent factor in the improved results obtained in the Johns Hopkins Hospital during the past 2 years has been the more adequate treatment of postoperative complications. Although this series of cases is small, the trend is in the right direction and serves to strengthen my conviction that immediate operation is the correct treatment for acute appendicitis in any stage of the disease.

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SOME LESSONS LEARNED IN THE GREAT WAR

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TO those of us whose fortune it has been to serve our troops in time of war, the spectacle of what is happening in Europe today cannot fail to make vivid again the memories of what we learned, and to stir within us anew a burning desire to help our heroic men. If we are to be truly helpful, however, we must make sure that we have really remembered the lessons we learned and that we are prepared to apply to present war conditions all the lessons that are new.

In approaching this important subject one is apt to succumb to the temptation to comment on every field of surgery with which one has had any contact whatever. Thus it is with difficulty that I refrain from referring to the remarkable things that we saw and did in the gunshot wounds of the chest, abdomen, and skull. On this occasion, however, I shall confine myself strictly to that field in which I have had a really broad experience and in which I should be able to speak with some authority.

Thinking over the compound fractures of the bones of the extremities, I would say that the greatest advance came from the introduction on the battle field or at the ambulance dressing station of adequate splinting. Everybody knows the spectacular reduction of the mortality rate that came with the introduction of the Thomas splint. Similarly there came a great improvement in the final results when the new methods of applying traction, such as by ice tongs, Sinclair's skates, and other devices were introduced. I have no doubt that further improvement will result from the Kirschner wire.

The outstanding impression left on my mind, however, from observation of large numbers of these patients at the convalescent stage, was the very great difference in the quality of the results obtained in different hospitals. The explanation was perfectly simple, for in one there was a leading spirit like Sinclair or Pearson or Blake whereas in another there was nobody interested in fractures. Surgeons had better get over the idea that anybody can treat fractures well enough, for the results that come from incompetent management are appalling. The remedy, of course, is to see that at least one expert in fractures is attached to each surgical unit.

The most important contribution to the treatment of wounds in the last war was the preliminary débridement followed by the Carrel-Dakin method of irrigation. Whether the latter will be superseded by the new methods remains to be seen. With regard to these, however, it would seem that if the bombing would allow a controlled experimental study of the new methods such as the Trueta occlusive treatment and the local and general use of the sulfonamide drugs, some definite conclusion should be arrived at before long. As things stand at present there is very little reason for confidence in the statements that are being made either for or against their use.

While practically all the compound fractures resulting from gunshot became infected, osteomyelitis was not a serious complication nor did it interfere greatly with the final result. Union went on in the usual way and often with greater osteogenic activity in the fragments than in simple fractures. Before my war experience it had always been my impression that infection was an important cause of nonunion. As an actual fact, however, of a thousand infected compound fractures that passed through my hands, less than 50 failed to unite and when one came to investigate these one found that the nonunion in most cases was due to loss of bone.

The most important lesson learned in regard to chronic osteomyelitis and septic nonunion was that the patients could be operated upon without any serious risk of stirring up the infection and that if the wound was left wide open with gauze drainage extending into its depths they rarely had a rise of temperature.

Oration on Surgery, presented before the Clinical Congress of the American College of Surgeons, Boston, November 3–7, 1941.

The contribution made by Winnett Orr when he pointed out the importance of wide open drainage, complete immobilization, and infrequent dressings cannot be overestimated. These wounds do not need to be dressed for 2 or 3 weeks and by that time are completely lined with healthy granulations and are well on the way to closure.

When the importance of this principle was thoroughly understood, a great change came into the treatment of the septic nonunions. Instead of limiting treatment to the infection and the osteomyelitis and waiting a year or two before attempting a bone graft operation, it became the general practice to deal with the nonunion at once by removing the sequestra, placing the freshened fragments in contact and immobilizing. The result in almost all cases was a quick union of the fracture and the saving of a year or two of hospitalization.

NERVE LESIONS

Of all the problems that the war brought to the reconstruction hospitals the most interesting was that of the lesions of the nerves. These cases were collected in special hospitals because in them the surgical staff was composed of men specially trained in extremity surgery and particularly qualified to deal with the deformities and disabilities that result from nerve lesions.

The rise of the neurological surgeon may lead to some agitation for a transfer of the nerve lesions from the orthopedic to the neurological surgeon, but from my observation of the two types of surgeon in action and from my own experience with both types of surgery, I would say that these patients are more likely to profit in the long run from the care of the modern orthopedic surgeon than from any other.

The lessons we learned about the wounds of the nerves were of the utmost importance and should be reviewed now if our young surgeons are to avoid our mistakes. Let me say that of all the remarkable things the surgeon does none is so spectacular in its results as the suture of a nerve. On the other hand no operation requires more attention to the details of technique if the best results are to be obtained.

Both in military and in civilian practice the question often arises as to whether a suture of a severed nerve should or should not be performed at the preliminary débridement. My answer is that if speed is necessary because of shock or hemorrhage or if there is the slightest risk of infection it should not be done. In clean incised wounds in which a thorough clean-up can be carried out it is justifiable, but in a shell wound, never. The business of the surgeon is to do a débridement as quickly and thoroughly as possible and to get the patient into an efficient splint and back to bed or on his way down the lines. The most that should ever be done to a severed nerve is to link the two ends with a catgut suture so that when the ultimate dissection is done the ends will be found close together.

The technique of nerve suture is well known, but I cannot refrain from referring to the absolute necessity of getting end-to-end contact if recovery is to be expected. To accomplish this all sorts of tricks must be resorted to, such as transferring the ulnar in front of the internal epicondyle and flexing the elbow acutely, flexing the knee to a right angle while repairing a 6 inch gap in the sciatic nerve and then placing the patient on his back with his hip in full extension and his leg dropped through a hole in the mattress so as to relieve tension on the sutures. In all these operations in which joints must be held flexed after the suture, a plaster bandage must be applied and left undisturbed for at least a month, that is, until the down-growing axis cylinders are well past the line of suture. After that a series of plasters must be applied at weekly intervals, and the joint straightened out gradually.

Occasionally the surgeon is confronted with a lesion in which the gap is so great that there is no hope whatever of bringing the severed ends into contact. If this happens in the musculospiral nerve it is of no great consequence because one can count on an extraordinarily good result from a transfer of flexor muscles into the extensors. But when it occurs in the median nerve it is a major calamity. Here there are three alternatives: First, one may dissect the nerve a long way back and then draw the two bulbs as closely together as they

will come with a silk thread, and close the wound. Ten days later the wound can be opened up and it will often be found that the ends can then be brought together without tension. Second, one may introduce a nerve graft. Theoretically this should be useful for it has been done successfully in animals, but in man the results have been disappointing. In no case in which I saw it done was the result worth the trouble. However, if I were working on these cases now, I would try out the suggestion of using degenerated nerve as a graft and freshening the distal end and the proximal end of the distal segment of the nerve when the axis cylinders were due to pass that point. This would at least be more hopeful than the third alternative, which consists of doing nothing.

AMPUTATIONS

Familiar as most surgeons are with the various types of amputations, not many have had a sufficient experience to justify the formation of final opinions on all phases of the question. It happens, however, that it has been the policy of the Canadian Government to bring all the amputation cases from time to time to an amputation clinic at the Government artificial limb factory at Toronto, so that it has been possible for a small group of surgeons, of whom I am one, to study and to follow these cases for nearly 25 years. A life history of all these patients, comprising 2,000 in all, is now being prepared by Dr. Gordon Dale and will be published soon. From our place of vantage in this clinic we have been able to observe these men, not for a week or a year, but for a quarter of a century. We have figuratively watched them walk down the years, slowly changing from youth to old age, and we feel that we know, as few can possibly have had the opportunity to know, the surgery of amputation.

I shall not attempt to discuss this matter in any detail as this has recently been done elsewhere. I must point out, however, a few outstanding principles that it would be well to remember if it is our misfortune to have to face again the casualty lists of 1918. Almost the only reason for amputating a soldier's limb is to save his life. It is because his limb is gangrenous or about to become gangrenous because of wildly spreading streptococcus or gas bacillus infection. It is seldom, therefore, that a formal amputation of any kind is justifiable. One must content oneself with a quick circular cut, leaving the skin long so that it cannot retract above the section of the muscles and bone and leaving the wound wide open for adequate drainage. This is the so-called guillotine amputation, modified by leaving the skin long, that became so popular in the casualty clearing stations and base hospitals in the old war. It was a life saver, pure and simple, but it worked.

One sometimes hears this type of amputation criticized on the grounds that it takes the stump a long time to heal, that it usually leaves a stump that is unsuited to fitting with an artificial limb and that it often requires reamputation. Admitting the truth of all these criticisms, however, we are still convinced that this method must be used if the mortality rate is to be kept down. Some modification of these views may come if the new bacteriostatic drugs prove helpful, but I doubt it.

It is in the reconstruction hospitals that final preparation of these patients for artificial limbs takes place and it is here that the formal amputations should be done. In the lower extremity, there are only four that need concern us as the others are practically only of historical interest. They are the Syme's and the midcalf operations below the knee and the Gritti-Stokes and the midthigh, above.

For nearly a hundred years the academic storms have raged about the operation of Syme. At one time it used to be the London surgeons who abused it but now it is said that Edinburgh has forsaken it and London has taken it up. Our experience has been, however, that it is the best of all amputations of the lower extremity and that when well done it allows a man to stand and walk all day, to follow the plough, to work in a factory or to do most of the things that a normal man can do. Twenty years ago I was put out of a squash tournament by a man who had had a Syme amputation done 15 years before. I met him the other day, 35 years after his operation, walking along with hardly a sign of a limp. It is our experience that if the heel flap

is well fitted on the ends of the sectioned bones, and if the nerves are cut well back, it will stand up to hard usage for a lifetime.

One of the chief causes of the unpopularity of the Syme operation has been the unfriendliness towards it of the artificial limb makers. Not many of them can make a good Syme artificial limb and even when they can they dislike it because it cannot be made symmetrical with the opposite limb. The result has been that whenever a Syme stump is the least bit defective, off it comes to make way for the pretty below-knee artificial limb. Unfortunately many a man has lived to rue the loss of his Syme stump for it is rare indeed for the midcalf below-knee stump to stand up to the wear and tear of ordinary usage the way a Syme's will do. The trouble with the below-knee stump is that with each step the whole of the weight is borne on the sloping sides of the upper end of the tibia, on skin that is unaccustomed to intermittent pressure and friction. The result is a succession of attacks of skin irritation, blistering, and ulceration. In not 1 in 10 cases can these men face anything but a sedentary life.

When the unsuitability of the midcalf operation for Canadian soldiers became apparent, all enthusiasm for reamputating Syme's stumps disappeared. It was quickly discovered that many of the defects could be overcome by doing the Syme operation over again, refashioning the flap, cutting short the nerves, and making sure that the bulbous soft tissue pad was held in correct relationship to the bones until healing occurred. Over and over again these defective stumps have been made perfect in this way and there is no doubt that before any Syme stump is amputated the possibility of repairing it should be thoroughly considered.

So unsatisfactory has the below-knee amputation proved in the Canadian army that the majority of these stumps, after a series of reamputations, removals of the fibula and excisions of neuromas have finally been converted into Gritti-Stokes above-knee end-bearing stumps. It is a pity, of course, to have to sacrifice the knee joint but experience has shown that the end-bearing thigh stump is far more serviceable to the workman than the midcalf. Large numbers of our men with this type of amputation are working an 8 hour day at benches and machines and seldom losing a day's work.

Compared with the other amputations that of the midthigh is a great calamity. In spite of the amazingly clever artificial limb that has been devised for it, it has been found that the men are rarely able to hold any but sedentary jobs. The trouble is that they have to sit on the top of the bucket, carrying weight on skin that is not accustomed to it and with only the minimum of control over the movement of the joints. It should be performed, therefore, only as a life-saving measure.

The dictum of Ambroise Paré that a gunshot compound fracture, combined with a rupture of the main artery to the limb, calls for amputation has stood for nearly 400 years. We are wondering, however, if after all this time some exceptions may not be found to this rule. Paré was faced with the certainty of infection piled on top of the fracture and the severe injury to the circulation so that he knew that his patient's only chance depended on an immediate amputation. With early débridement of wounds, however, infection can be completely prevented in many cases and the new drugs may ultimately increase this number. It may be possible, therefore, with the aid of heparin, to restore the circulation at the time of the débridement by suture of the severed artery or to maintain it for a few days by means of a glass tube, until a collateral circulation is established. Certainly the experimental studies of Murray both on animals and on a small series of patients in hospital indicate that occasionally, particularly in air raids, when the patients can be brought quickly to hospital, such a plan of treatment might be effective.

While in this review of experiences gained in the war of 1914 I have limited myself to a very small part of the broad field of war surgery, much of what I have said has close relationship to all wounds, no matter where they may occur. What we all want to know is, first, how to prevent wounds becoming infected and, second, if they are already infected when they come into our hands, how best to combat that infection and to give our patient

the best chance for his life and limb. From the old war we learned or relearned the importance of splinting, débridement, and free drainage. In this war we shall have an opportunity to try out the effectiveness of chemotherapy and the use, locally, of the sulfonamide group of drugs. If medical experience in this war in any way resembles that of the last, however, the process of arriving at sound conclusions on these matters will be exceedingly slow. It seems to me that the information we so urgently need can come only from large scale controlled clinical experiments such as have been proposed by Meleney of New York. If, for instance, groups of 50 street accident cases were placed under the observation of a few trained observers and if one group were treated by débridement alone, one by débridement plus Carrel-Dakin irrigation or chemotherapy or the local use of the sulfonamides or the Orr-Trueta occlusion method, it should be possible within a few months to settle the question of how to treat wounds. Such experiments could easily be carried out in the great hospitals of New York, Chicago, and Boston, supplied as they are with enormous numbers of patients and sheltered from the continuous disruptive effect of falling bombs. What a grand thing it would be for our soldiers if, before the great casualty lists begin, the Director General of Medical Services really knew the value of the new methods of treatment and felt himself so strongly supported by experimental and clinical evidence that he could order the adoption of those general principles that offer the greatest hope of success.

I cannot conclude my remarks without thanking you for the high honor you have done me in adding my name to the list of the distinguished surgeons who have delivered the "Oration on Surgery" before the American College of Surgeons. I must confess that the word "oration" at first filled me with misgivings; but I find that it really is a word which is used, not to cramp the style of the speaker, but to do honor to him. Allow me at this moment, too, to assure you that the kindly and friendly spirit which has led you in this time of war to select a Canadian as your President is deeply appreciated by myself and my colleagues. The overwhelming evidence of your friendship brings comfort to all Canadians and helps them to face the future with good heart, no matter what that future may hold.

THE PROBLEMS OF SURGERY IN TOTAL WAR

With Special References to Abdominal Injuries

Temporary Surgeon Rear Admiral GORDON GORDON-TAYLOR, C.B., O.B.E., LL.D., M.A., F.R.C.S. (Eng.), London, England

I PROPOSE to make use of a certain series of abdominal injuries collected from the casualties of this war, and to employ this group of cases as a means of introduction to the consideration of certain clinical phenomena which appear to be novel in this conflict, to certain methods of treatment which are on trial, to the great value of whole blood and the blood substitutes which have been employed on an unprecedented scale in this campaign, and finally to the environment in which many of these patients have been injured or dealt with surgically.

The most prolific cause of injury throughout the centuries has been the warring instinct of mankind. Heretofore, the male has naturally been the sex almost exclusively marked out for this type of lesion; but "total war" makes no sex or age distinctions, and the experience of the Spanish war, which was utilized by Nazi and Fascist merely as a dress rehearsal for the blood bath to be commenced in the autumn of 1939, should have warned mankind of the principles and practice of the aggressors, nay assassins, who are now engaged in endeavouring to institute in Europe what has been inappropriately termed the New Order—surely a most glaring misnomer. Among the more primitive tribes it is almost unknown for the male deliberately to attack or injure the female; and in the animal kingdom it is only on the rarest occasions that the male has made an onslaught upon the female of the species. The wholesale, indiscriminate bombings, involving the lives of countless women, children, babes and sucklings which characterize "total war," forever brand those nations who first introduced and practiced this technique with the stigma of a reputation for diabolical cunning, cruelty, and sheer blood-lust unknown in any brute or beast.

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In ancient times surgeons built up their experience in the workshops of war; and war throughout the ages seems always to have served as a stimulus to advancement in surgical knowledge and craft. It is a little strange that the abdominal surgery of war should have lagged so far behind the operative treatment of similar injuries received under peacetime conditions. Six centuries have rolled past since Henri de Mondeville counselled suture of the colon and affirmed the recovery of some of those who had received wounds of the large intestine, and Ambroïse Paré in the sixteenth century, writing of prolapsed and damaged intestine, pointed out that the injuries must be sutured, and evisceration reduced.

The dismal story of the lack of surgical progress in the abdominal surgery of battle, which characterized the centuries up to the period of the last great war, is well known and need hardly be reiterated. The present occasion, however, affords an opportunity for correcting at least one error respecting the history of the abdominal surgery of the war of 25 years ago. If I may be permitted to digress for a moment to the history of the abdominal surgery of that great conflict, the first abdominal operation on the Franco-British front was in fact performed in December of 1914 by the late Captain John Campbell of Liverpool, an alumnus of a famous school of abdominal surgery; the operation was a successful suture of a penetrating wound of the stomach.

The work of Owen Richards, however, really placed the abdominal surgery of warfare on its permanent sound footing. His enthusiasm and enterprise were fittingly crowned by the honor of being the first surgeon on the British Front to save an intestinal wound by means of operative surgery. On March 18, 1915, this surgeon successfully excised six feet of ileum,

perforated in twenty places; in some parts the gut was so damaged that two-thirds of its circumference was torn through. The soldier was a Scotch Canadian, who, after receiving the injury in a German trench, walked back to his own lines.

The third successful abdominal operation on the British Front in the last great war was performed by Claude Frankau and dealt with a gunshot wound of the colon. Here are recorded three pioneer operations: stomach, small gut, colon; Campbell, Richards, Frankau.

No story of the abdominal surgery of warfare would be complete without some reference to Sir Cuthbert Wallace, whose enthusiasm and staunch support for his surgeons in the British First Army in the war of 1914–1918 did so much to settle forever the curious controversy upon abstention or intervention for abdominal wounds which had occupied the minds of military surgeons so long. No quixotic fancy made me write a year or two ago: "St. Cuthbert must surely be adopted as the patron saint, not only of the luckless stricken in the belly by the missile of an adversary, but also of all such surgeons as have a special interest in the abdominal injuries of warfare."

After 2½ years of warfare, it is perhaps not inopportune to take stock of our experience of the abdominal war injuries of this "total war," and to compare and contrast the war surgery of the abdomen of two periods of time separated by a quarter of a century.

The series of 600 operations for abdominal injury in this present review comprises a most motley collection, including abdominal casualties received in naval warfare or admitted into Naval institutions, and civilians damaged by the indiscriminate air bombardments of Britain; there are also included certain Army casualties, represented by the abdominal flotsam and jetsam of the "Dunkirk miracle" and the evacuation of northern France. Still others come from the Royal Air Force and are for the most part those brought down during the epochal "Battle of Britain," which should be surely termed the "Battle over Britain"—a nomenclature which perpetuates for all time the prowess of "the few to whom so much has been owed by so many." This multifarious group constitutes a series from which conclusions may justifiably be drawn.

In addition, there are also cases of injury to the belly which have been received under circumstances more or less inseparably related to "total warfare"; thus for example, the "blackout" has played no inconsiderable part in determining abdominal damage of this kind. Novel environment has also led to disasters, some of which involve the belly; the spleen has been ruptured through a fall on the stone floor from an air raid shelter bunk (!), by the fall of a warrior on his tin hat or of a sailor upon his gas mask. Catastrophes which befall the individual in peace may also overwhelm him in war, and the circumstances of the emergency and the environment of operation may invest both with a panoply of the dramatic.

Abdominal catastrophes consequent upon disease have also been dealt with surgically under "front line conditions"; perforated peptic ulcers have been dealt with successfully by operation in hospitals during air raids, and even in the woods adjacent to the Dunkirk beach. Strangulated hernias have been admitted along with air raid casualties during the "blitz," and have taken their turn for operation with men and women injured by high explosives.

ABDOMINAL SERIES

Infrequency of operation. In this present conflict the abdominal surgery of war has certainly seemed conspicuous by its infrequency, and the apparent paucity of numbers has impressed individual observers whose sphere of surgical activity in the Franco-British Casualty Clearing Zone 20 odd years ago furnished them with an abundant experience of operative aid for soldiers suffering from wounds in the abdominal area.

In Great Britain, no one hospital, no single surgeon, has had so far any vast experience of these cases; they are scattered over innumerable cities, townships, villages, and hamlets throughout the land. The conditions of wounding today are of almost infinite variety, and in this "total warfare" the men of the fighting forces and the civilians, the women and children, the aged and the nursling have

suffered injuries to the belly and elsewhere in circumstances as diverse as the missiles and mechanisms of destruction that have damaged, destroyed, or perhaps completely dissipated their bodies.

In this "total war" a considerable percentage of the casualties from air bombardment results from crushing force or from the direct or indirect effects of "blast"; in crushing injuries the abdomen is less exposed to damage than, for example, the head, shoulders, or limbs; and in lesions due to "blast" the lungs are more vulnerable than the abdomen. Experience has in fact demonstrated that, despite the stout-hearted efforts of rescue squads and the courage and devotion of ambulance drivers in cities, desperate or moribund abdominal cases do not crowd the doorsteps of our hospitals and infirmaries, and it becomes difficult to escape the conclusion that in Britain at any rate abdominal casualties able to repay surgical aid are in truth infrequent.

The infrequency of abdominal operations among civilian casualties. The following considerations are germane to the discussion.

1. The frequency and severity of crush injuries of the trunk, including the abdomen, have been a feature of casualties on the "home front"; such injuries are indubitably more mortal than penetrating wounds. Subparietal injuries of the abdomen and its contents played a relatively small part in the abdominal surgery of the last war; this time civilians, women, and children of tender years, and even the unborn babe, are suffering crush-contusions from falling masonry and from burial under collapsed houses and dwellings. Fragments or masses of wood, stone, or metal may be confusedly hurled with devastating force against the abdomen; severe visceral damage or retroperitoneal hemorrhage may be produced by "blast" without any external evidence of injury. The abdominal parietes may suffer along with the subjacent organs, and effusions of blood may be encountered in any of the layers superficial to the peritoneum. Actual rupture of the abdominal musculature along with visceral injury was infrequent in the last war; the blow that ruptured the powerful belly muscles became too spent to damage the intestinal tract. The increase of destructive force nowadays destroys and damages without fine anatomical distinction.

2. In towns and villages the most frightful wounds of the belly have been produced by flying glass; abdominal casualties have been eviscerated, or festoons of damaged intestine may be herniated in front and behind, along with other injuries inside the peritoneal cavity. Such are mostly beyond surgical aid.

3. Multiplicity also characterizes the wounds and damage sustained from air bombardment; not only is the mortality raised by concomitant lesions of many viscera, but many, even most of the regions of the body may be simultaneously damaged. The metal and dirt bespattered trunk and limbs in those who had been wounded by high explosives were familiar to surgeons in the last war, but the phenomenon is far more frequent in this conflict, and the severity of the accompanying injuries renders the prognosis in many an abdominal case hopeless.

4. Some of those injured in the belly may also suffer from burns of the body or limbs. This complication of abdominal injury may be encountered in ships or ashore; the prognosis will obviously become far more grave in such cases.

5. The degree of shock encountered among the casualties of this war far transcends that with which surgeons were familiar between 1914 and 1918. Despite the elaborate and highly organized resources of transfusion services, despite the transfusion of many pints of blood or plasma, despite the administration of oxygen, and all the resources of resuscitation therapy, many of the patients with abdominal injuries are past all operative assistance.

6. The clinicopathological phenomena found in men or women exposed to "blast" have been reproduced experimentally by Zuckerman (1940), who has shown that in 40 per cent of experimental animals subjected to "blast" hemorrhagic lesions are found in various abdominal organs. In the realm of human pathology and in experimental work the abdominal viscera appear to be less sensitive to "blast" than are the lungs, and ex-

perimentally in cases in which lesions are present in the belly there are also pulmonary hemorrhages. The special vulnerability of the large intestine to "blast" in the case of the experimental animal is not so marked in the case of men and women; the proclivity of the small gut to exhibit lesions due to this casual mechanism is not far inferior to that of the large bowel; the stomach is seldom affected. The intestine may exhibit patches of hemorrhage varying from punctiform spots under the serosa to large annular extravasations, and even rupture of the bowel has been known to occur.

The spleen may be torn in persons exposed to "blast"; the liver has been bruised or torn, or its right lateral surface may be diversified by lines corresponding to the ribs; the kidneys and bladder are less often implicated. Blood clot has been seen in the peritoneum, and retroperitoneal hematomas, as well as effusions in the mesentery, are very characteristic. Attention is specially directed to these findings in the abdomen which result from "blast," but once more it should be affirmed that the lungs are especially vulnerable to this mechanism, and that the planes of the head and neck and the nervous system may exhibit similar and perhaps extensive changes. The direct effects of "blast" are experienced close to the explosion only, but the many indirect effects may produce death or serious injury at a further distance.

Nevertheless, apart from the actual nature of the abdominal wound, the "time lag" between the hour of wounding and the possibility of expert surgery in a suitable environment obviously plays a most important part in determining the fate of all abdominal casualties not immediately fatal.

The infrequency of abdominal casualties in the forces. The possibilities of the rapid collection of the wounded, and their rapid and efficient transport so as to keep the "time lag" within permissible limits must vary with the naval or the military situation. The time factor may be inevitably protracted to the grave disadvantage of the patient by the vastness of the intervening expanse of sea or air.

In army warfare a prolonged "time lag" should not be so inevitable or capricious save in circumstances of retirement, since hospitals reserved for the treatment of abdominal and other cases of "first urgency" should be so mobile that they can be kept within the permissible "time lag" despite the rapid movements which nowadays characterize war. Alternatively, under certain conditions air transport can surely bring surgeon and patient together with the least sacrifice of important hours.

It is manifestly impossible to maintain forward hospitals in an army falling backward, especially under conditions of rapid retreat. All patients operated upon before the "break through" must be sent far rearward, and for the most recent casualties little more than first aid treatment is possible before evacuation. Such untoward circumstances obviously preclude the possibility of recovery for any large percentage of abdominal cases; those that survive owe more to their own physical stamina and stoical fortitude than to the exuberant optimism and enterprise of the surgeon. Abdominal casualties certainly survived the retreat of Gough's Fifth Army in March, 1918 and also the more recent Dunkirk evacuation.

In the first clash between the British forces and the enemy across the Channel in May, 1940, the military situation precluded the successful performance of abdominal surgery, save on a small scale. Cases are known to me of abdominal injuries received during this period of very mobile warfare in which patients were operated upon in France and Flanders, were rapidly embarked at Dunkirk and other French ports, and completed their recovery in England. For example, Major W. E. Underwood, R.A.M.C., had several successful abdominal cases at this time.

Nowadays, the conveyance of British wounded in hospital ships under the aegis of the Red Cross carried special dangers. Abdominal casualties during transportation across the Channel and the high seas have shared with other injured men the mental torture and perhaps further physical agony from deliberate bombardment of the Red Cross.

In this war the chances of recovery of an abdominal case from such an outrage have been prejudiced still further by the air bom-

bardment of wounded men in the water, a practice which has been freely indulged in by the German and Italian even upon Axis allies, and few that had already been wounded in the belly can have survived.

By reason of the environment in which naval casualties are inflicted and the nature of the missiles employed, abdominal wounds are very fatal in ships, although some splendid results have in fact been obtained in men wounded at sea, or even in the sea, during this present conflict. Surgeon-Lieutenant Donald, R.N., performed a laparotomy in one of H. M. Destroyers, when the "naval situation" was such that there was no prospect of transference of the man to a hospital ship or ashore. Unfortunately, the cecum and ascending colon proved to be gravely damaged, with extensive contamination of the peritoneal cavity with liquid fecal material; the man succumbed. An injury to the small bowel might have held out a better hope of recovery.

Immersion in the sea after shipwreck has on occasion been associated with a less familiar abdominal injury, to which Surgeon Commander Rex Williams, R.N., has given the name "immersion blast." This will be referred to later in the author's forthcoming Bradshaw Lecture and in Rex Williams' Hunterian Lecture in 1942.

Nowadays there is no safe sanctuary anywhere for the wounded, even in the hospitals and infirmaries of our cities. Wounds from enemy aircraft may even supervene upon medical illness; the Boche never hesitates to hit again when man, woman, or child is down. The destruction of hospital buildings may withdraw from the wounded man the hand stretched out to save him; every hospital in London except two has been hit by indiscriminate air bombardment. A police inspector had been wounded by a bomb splinter which had entered the right flank, presumably damaging some intraperitoneal organ. He was placed upon plasma infusion which rallied him, and the man would without a doubt have been able to be operated upon; unfortunately, the hospital was badly damaged with loss of life to nursing sisters and others, and it became impossible to operate or for a time to evacuate. The man succumbed.

Sex. In figures culled from air raid casualties in Great Britain, there is no striking difference in incidence between the sexes. However in one series of abdominal cases in which I have taken particular interest, but *which is a motley collection*, 78 per cent were men, 20 per cent women, and 2 per cent children. Nine of 11 of the infants injured in this series were girls.

Age. The youngest victim in this abdominal series to survive an intraperitoneal injury due to enemy action was aged 3 years; this was a subparietal lesion. The next youngest to survive were 7, 8, and 9 years of age, respectively; the mortality in babyhood and early childhood is extreme, although a baby of 10 months recovered from a through-and-through wound of the abdominal wall, which did not implicate the peritoneal cavity.

The following cases perhaps emphasize the horrors of the modern technique of air attack introduced by the totalitarian powers:

A girl of 11 years walked into a hospital, close to which she had been injured by a bomb splinter. She had a penetrating wound of the abdomen situated near the right costal margin and bleeding profusely. At operation, no injury to the gut was found, but there was a severe tear of the right lobe of the liver The tear was partly sutured and also packed. Despite every form of treatment the wounded girl continued to bleed, and died 24 hours after operation.

The injury from which a little girl of 3 years made a recovery was a subparietal lesion and probably involved an injury to the common bile duct. Her life had been despaired of for several days after she had been rescued from a house in a row which had been completely demolished; she then developed a huge collection of bile in the lower part of the belly; this was drained and convalescence was then straightforward.

A girl of 8 years was an in-patient of a hospital for an operation for cleft palate. During her stay in hospital, the building was badly bombed by Huns, and she received a small perforating wound near the middle line at the level of the third lumbar vertebra. She was hurriedly removed from the damaged building to another institution, and two perforations in the sigmoid flexure were sutured A proximal colostomy was performed. Recovery took place.

A boy of 9 recovered from a frightful left-sided abdominothoracic injury in which his stomach was protruding from the wound (Alcock).

The youngest living thing known to be destroyed in the maternal womb was a fetus of 6 centimeters! A woman was in an air raid shelter which was destroyed and was thought to present the clinical

picture of a blast injury to the lungs. After 48 hours, she succumbed, and at the autopsy the clinical diagnosis was confirmed by the pulmonary changes demonstrable. She had also a large retroperitoneal hematoma, especially marked in the perinephric regions; there was an extensive blood infiltration of the mesentery, which had encircled the bowel under its serous coat in several annular patches. The uterine cavity contained some blood, and there was a partial separation of the placenta from the uterine wall. The fetus measured 6 centimeters in length, and showed a bruise on its anterior abdominal wall—surely the earliest living thing to receive a blast injury.

After 12 years of age, the prognosis seems to be less dismal.

A girl of 12 was running in the open to an air raid shelter, when she was struck by a flying piece of metal. She had a punctured wound of the left paraumbilical region, through which some omentum had been extruded. At the operation (Mr. Donald Thompson) tears were found in the small bowel and transverse colon. The missile was extracted from the rent in the large bowel. The gut injuries were treated by suture. An uninterrupted recovery took place.

Phoebe C., 15 years of age, was admitted to hospital in a state of extreme shock resulting from wounds received from bomb splinters. There were multiple wounds of the back, and a large laceration of the left buttock tracking up between the sacrum and ischium and penetrating the abdominal cavity. Ten hours elapsed before she could be made fit for surgical exploration of the abdomen. She had 7 perforations of the small gut. A large piece of metal was removed. Recovery took place (Mr. Lloyd's case).

At the other extreme of life *old age*, although naturally increasing risk, does not preclude recovery.

Male, 71 years, received penetrating wound of abdomen; 3 perforations of small bowel; lacerated wounds of scalp and left eyelid; abrasions of face, scalp, and hands (Mr. Southam's case). This man, despite his years, made a surprisingly smooth convalescence. A plastic operation upon his scalp was successfully performed a month later.

Annie M., aged 73, recovered from a left-sided abdominothoracic wound; fortunately no abdominal viscus was injured. The woman, however had a fracture of the fourth rib on the left side; and there were lacerations of the right forearm, right breast, and left elbow.

Abdominal injuries of "total war" and pregnancy. It is a ghastly commentary on Nazi *Kultur* that their deeds should have made the record of the following cases possible:

E. S., 20, unmarried, 4 months pregnant, received a bomb injury of the abdomen. Two severe lacerations of right arm were excised and treated by local chemotherapy; there was also a wound in the right iliac fossa. A glass splinter 3 inches by 1 inch was found lying loose on the cecum; no internal organ was damaged. The abdomen was closed without drainage. It was "just too bad" that the patient did not miscarry (Major Rodney Smith's case).

A married woman 5 months pregnant was injured by the explosion of a bomb in close proximity, but never attained a condition permitting operation. The fragment had entered the left labium majus, fractured the left ascending ramus of the pubis, driving a fragment of bone into the bladder; the missile then traversed the pregnant uterus, contused the cecum, and was finally arrested in the right sacroiliac articulation. Her daughter, aged 7 years, simultaneously received a right-sided abdominothoracic wound implicating lung, diaphragm, and liver; the girl recovered.

A woman of 21 years, 8 months pregnant, was admitted to Hospital with a bomb splinter wound of the left side of the abdomen, through which part of the omentum was protruding. Shock was profound. At operation (Mr. G. H. Baines' case), several perforations of the small intestine were sutured; considerable intraperitoneal hemorrhage was present. In view of the patient's desperate condition the abdomen was closed with through-and-through sutures as hastily as possible. Stillbirth took place the following day. For the first week following operation the pulse ranged round 120; the abdomen was greatly distended. On the tenth day the patient had a pulmonary embolism. After this, convalescence was smoother, although protracted, and she was finally discharged from hospital on the seventieth day.

A woman, 9 months pregnant, was admitted to hospital with multiple injuries which resulted from a bomb explosion. The left buttock was completely destroyed; a piece of omentum was hanging out of a wound in the belly wall. The patient died without operation.

A woman of about 35 years, 9 months pregnant, was admitted to hospital gravely ill, with a severe fracture of the skull from which brain matter protruded. Shock was extreme; the fetal heart sounds were still audible. It was apparent that the patient was going to die, and the question of cesarean section was mooted. The prospective father and every member of the family had been killed by the same "incident," and no operation was performed.

Abdominal injury due to enemy action during parturition. Enemy air raid activity may not only produce abdominal injury in the parturient woman, but naturally injuries in other parts of the body may be produced.

The good fortune, so far as loss of life is concerned, of the well known historical maternity hospitals in London has been remarkable. All have suffered as a result of enemy

action, but no patient has actually been killed within their walls. In another institution the abdominal wall of a patient was ruptured during labor pains, as the result of "blast."

Alice G., aged 36 years, 9 months pregnant multipara, was in the maternity department of a hospital. She complained of labor pains one afternoon, and by evening the pains were strong and frequent. During a severe air raid at night, when several flares lit up the building, she got out of bed and walked along the corridor. At this moment a heavy bomb fell in the hospital grounds about 150 yards from the maternity ward, and all the windows and most of the ceilings in that portion of the hospital were damaged.

The patient collapsed, and examination revealed a loop of transverse colon protruding from a rent in the upper abdomen. This wound was vertical, 4 inches long, and situated over the outer border of the right rectus; the edges were clean cut and bloodless; the bowel was not perforated. There was no evidence of her nightgown having been torn by bomb splinters or glass. A forceps delivery was performed 3 hours after the incident, and a stillborn female child was obtained; the extruded bowel was then replaced. Despite every form of resuscitation the patient died 2 hours later.

Nature of projectile producing injuries. In discussing the nature of the projectiles, it has already been emphasized that many of the injuries received from air bombardment are subparietal or nonpenetrating in character. In the majority of the series of abdominal cases which were selected for special study, a fragment of bombcasing has been the projectile. Certainly in no abdominal case has a large retained fragment of metal been encountered; the largest retained fragment in a patient who recovered was the size of a walnut. In a number of cases the injuries have been produced by bullets: on the whole, these have done well. The increased use of the incendiary bullet adds to destruction and necrosis of tissue produced by burning; in the case of the intestine this may demand resection, where suture would otherwise have sufficed. The recovery rate of those injured by the revolver bullet is flattering to the surgeon.

The destructive effects of flying glass in air bombardments are nowadays familiar to most surgeons. It suffices merely to mention the tragic facial disfigurements in women, the damage or loss of eyes; while in the abdomen coils of intestine may be cut to pieces within the belly, or may hang out of dreadful gashes in the chest or abdominal wall. A man admitted to hospital wounded by a long spicule of plate glass had the hepatic flexure of the colon and a coil of small gut completely divided; his right kidney was cut in sunder, and the continuity of the renal vessels at the hilum; the man died despite operation.

Small puncture wounds produced by glass may betray catastrophic lesions within. A blood stain on a woman's night dress revealed a small punctured wound in the epigastrium. On wiping away a clot which had temporarily sealed the small wound, a column of blood a foot high spurted upward. A splinter of glass of the size of the index finger was withdrawn from the liver. The patient succumbed.

Sometimes visceral injury produced by glass is less severe, and lesions of the bowel have been successfully treated by surgery. Sometimes, there may even be peritoneal penetration, without visceral damage.

A patient may be wounded by glass *and* bomb splinter; for example, a man had numerous punctured wounds all over the body due to glass; one tiny puncture was situated just below the left costal margin. There was no shock, but lower abdominal pain and infinite tenderness below the umbilicus.

Operation was performed by Mr. Meyrick Thomas and Mr. Desmond Cooper. After excision of the wound, when the track was followed inward, it appeared definitely to end at the level of the external oblique aponeurosis. However, when this was incised the track was found to pass through the internal oblique and transversalis, and a tiny puncture wound in the peritoneum. The peritoneal cavity contained a quantity of blood; small wounds in the anterior and posterior walls of the stomach were sutured; a small retroperitoneal hematoma was found, and a spurting artery in the position of the coronary artery where it was just leaving the posterior abdominal wall to enter the lesser omentum. Subsequent x-ray examination showed a small dense fragment low down at the level of the lumbosacral junction. Recovery took place.

A man received a double injury under unusual circumstances. When milking a cow, he was hit in the upper part of the buttock by a bomb splinter and gored in the thigh by the animal! He was found to have two perforations of the small bowel, which were sutured; the cecum was "grooved," but not perforated. There was a wound of the right anterolateral surface of the bladder, and the fragment was found in the

vesical cavity. The thigh wound inflicted by the cow was very extensive. The man made a good recovery (Mr. M. D. Shepherd's case).

In addition to glass fragments, débris, stones, and mud, other foreign bodies may be met along with bomb fragments.

A man standing in the street received abdominal injuries from a bomb splinter; the wound of entry was situated under the left costal margin, the wound of exit in the lumbar region to the left of the spine. Operation revealed a complete severance of the transverse colon; a bomb splinter and 2 pennies (!) were removed from the track. Unfortunately, the man died.

Viscera may be damaged by in-driven bone fragments, although the missile itself does not penetrate the peritoneal cavity. This has happened especially with fractures of the innominate bone, sacrum, ribs, etc.

Hollow viscera have been punctured by metal fragments which have not penetrated the peritoneal cavity. Cases of bowel injury by indirect violence were reported by Owen Richards, Sir John Fraser, and others in the last great war. One such case had both recti abdominis almost completely divided by a through-and-through wound, which was explored and the peritoneum was found intact. Nevertheless, the man succumbed and 3 lacerations in the small intestine were present; the injured piece of bowel lay immediately underneath the wound of the abdominal parietes. Similar cases have been met with in this war, for example:

E. N., female, aged 43 years, was admitted to hospital half an hour after being wounded by a high explosive bomb. On admission, shock was found to be only mild; there was a deep laceration of the right groin just below Poupart's ligament, which appeared to involve the tissues behind the ligament and also the extraperitoneal structures of the right iliac fossa. There was no wound of the abdominal wall itself, and no evidence at first of any intra-abdominal lesion. Three hours later, tenderness and rigidity had developed on the right side of the abdomen, and a laparotomy was now clearly indicated. At operation (Mr. Wass) it was definitely established that no communication existed between the wound in the groin and the celomic cavity. Nevertheless, 3 perforations of the lower ileum were found to be present.

There are only two bayonet wounds in this series.

An enemy agent, during the Dunkirk evacuation, was bayonetted through the right lower chest in the "black-out." There was a lacerated wound of entry over the ninth right rib, which was fractured; the wound of exit was situated in the right hypochondrium anteriorly. There was considerable abdominal tenderness, but apart from the excision of the wounds of entry and exit, the man was treated on conservative lines; he recovered (Major A. S. Till's case).

F. P. (Mr. J. S. Horn's case), aged 24 years, a soldier, was sent to hospital with the history that he had fallen on his bayonet while at practice. The bayonet had been removed from the left ischiorectal fossa where it had entered, and a stitch had been put in the skin as the bleeding had been profuse. There was a small exit wound in the left subcostal region. He was very shocked and given a pint of citrated plasma, followed by a drip transfusion which was continued during the operation. At laparotomy the spleen and left kidney were found to be uninjured, but there was a small hole leading from the peritoneal cavity into the base of the bladder. The bladder was therefore opened, and an attempt was made to suture it, after which both the bladder and the peritoneal cavity were closed with drainage. The wound in the buttock was sprayed with sulfanilamide powder and drained, as was also the wound in the side. After a somewhat stormy convalescence, he recovered.

Immunity of viscera in penetrating injuries of the abdomen. The occasional immunity of viscera in penetrating wounds of the abdomen first suggested in the South African War, confirmed in the last great war, has again been re-established.

Spontaneous recovery from indubitable wounds of the hollow viscera which was demonstrated by Makins, Cuthbert Wallace, Green-Armytage, Gordon Bell among British surgeons in the last great war has been confirmed by the experience of today.

The buttock wound. In 59.6 per cent of penetrating wounds of the belly, the wound of entry is anterior. In 40.4 per cent, the wound of entry is on the posterior aspect of the body. In half of these (20 per cent of total) the wound is in the buttock. The dangers of overlooking the buttock wound were stressed in the last war; the great frequency with which this constitutes the portal to the peritoneum emphasizes the necessity of completely stripping the patient and the most thorough examination of the whole body.

J. S. (Mr. Greening's case), aged 23 years, "danseuse," had been treated intermittently for syphilis since 1937. In the beginning of 1941, her Wassermann

was ++, and she was under treatment when she was wounded by a fragment of bomb. The patient, in addition to intravenous injections, had also received a very large number of injections of bismuth in the buttocks. On January 11, 1941, it was the left buttock that the missile entered, passing upward and across the abdomen to the right iliac fossa. She made a satisfactory recovery from an operation which comprised a resection of 6 inches of ileum and the suture of two other perforations of this portion of bowel, as well as the suture of a wound in the bladder. Her courage and pluck were such as to stimulate her to return to the "West End of London" 4 weeks after her operation. She had discharged herself from hospital against surgical advice. Subsequently, she required treatment for the removal of sequestra from the innominate bone, and for an infection of her bladder with Bacillus coli and Bacillus pyocyaneus.

Direction of missile track. Wounds which track across the abdomen *from side to side* enjoy a more sinister reputation than those whose direction is anteroposterior.

The case of a very successful result is recorded as follows:

A member of the Home Guard (Mr. F. H. Bentley's case) was accidentally shot through the abdomen by a rifle bullet, sustaining 13 perforations in small intestine. The abdomen was opened 4 hours after the injury, and after the intravenous administration of 2 pints of blood, and was found to be completely filled with blood. The bullet had splintered the ilium and was lodged in the left iliacus; the hemorrhage had largely proceeded from the laceration of the pelvic mesocolon. The continuity of the small bowel after resection of 4 feet of damaged jejunoileum was effected by an end-to-end junction. An uninterrupted recovery ensued.

The vertical wound track had also a bad reputation in the last war; many specimens in the former collection at the Royal College of Surgeons illustrated the truth of this statement.

A case with a successful outcome occurs in this present series:

A woman, Ethel K., received a penetrating wound of the left buttock. An x-ray film showed the presence of the fragment high up under the cupola of the diaphragm. There was a quantity of blood in the celom, and there was much retroperitoneal bruising, and hemorrhage in the left iliac fossa. Two perforations of the jejunum were sutured. The patient made a good recovery.

The large wound involving one of the cavities of the body is nearly always fatal; the man with a large wound of the abdomen or a wide loss of the abdominal wall seldom recovers.

A patient was admitted to hospital with an extensive abdominothoracic injury, including a large perforating wound, 8 by 4 inches in the left lower chest and left hypochondrium, associated with a pneumohemothorax, a lacerated diaphragm, and a perforation of the splenic flexure of the colon; he lived 5 days after operation, *dying* of pneumonia. The lower 6 ribs were fractured on the left side, and the fractures were implicated in the huge wound. There was also a second wound of the thoracic wall 3 by 3 inches which involved only skin and muscle. The capsule of a sclerotic spleen was torn, but had not occasioned hemorrhage; no treatment for this was needed. The torn diaphragm was sutured to the parietes with improvement in respiration and general condition. The dimensions of the wound and loss of tissue precluded its complete closure.

A man admitted to hospital after injury from a bomb had the anterior abdominal wall, including the peritoneum, completely torn away. Numerous pieces of rubble of varying size covered the presenting intestinal coils. There was a complete rupture of the transverse colon and several perforations of the jejunoileum. Mr. Desmond Cooper, working at top speed, brought the two ends of the damaged colon to the surface, sutured the perforations of the small gut and made a gallant attempt to close as much as possible of the anterior abdominal hiatus. Despite the fact that the operation was completed in 15 minutes and all the resources of transfusion therapy employed, the patient succumbed.

This dismal story might be told and re-told almost indefinitely; nevertheless, some wonderful recoveries have taken place and constitute veritable triumphs of surgical skill.

Mr. Arnold Alcock's case is perhaps specially remarkable, inasmuch as the boy was only 9 years of age:

A boy of 9 years was admitted to hospital with a large wound 8 inches long in the lower part of the left thorax; fifth, sixth, seventh, eighth, and ninth ribs were splintered, and there was a tear in the diaphragm 4 inches long. From this traumatic chasm the stomach protruded; there was a small puncture wound on the lesser curvature which was fortunately not large enough to permit the contents of the replete viscus to flood the thoracic and abdominal cavities. There were also several incomplete tears of the gastric wall, produced by the fractured ribs. The lung appeared undamaged. The perforation in the stomach was enlarged, and a mass of undigested vegetables emptied from its cavity; the gastric wound was sutured. After a thorough excision of the wound, the diaphragm was sutured, and the thoracic wall closed; a Malecot catheter was introduced into the pleura through a separate incision posteriorly. After an anxious week, the patient's progress was maintained and he made a good recovery.

A seaman (Mr. John A. McLauchlan's case), of 40 years of age was admitted to hospital for injuries due to a bomb fragment. There was a large wound, 8

inches long, over the eighth, ninth, and tenth ribs on the right side just above the costal margin. The seventh to eleventh ribs inclusive were fractured and stove-in. The pleural cavity was opened, the diaphragm torn, the upper surface of the liver lacerated, and the upper pole of the right kidney punctured. The wound was excised, the liver sutured, diaphragm repacked. The jagged and comminuted ends of the broken ribs were removed, and the diaphragm was attached to the thoracic wall above the rent. The chest was closed in layers. Recovery took place.

Nonpenetrating or subparietal abdominal injuries. Careful postmortem investigation disproves the belief that fatal casualties without external wound are frequently abdominal injuries. In only about 10 per cent of all fatal casualties in one series of cases could death be attributed to an abdominal lesion; a primary blast effect could only be impugned as the causal mechanism in a tiny fraction of these. Most of the abdominal lesions among these fatal cases were caused by collapse of buildings, and crushing injuries; or by blows upon the belly by flying missiles or portions of collapsing buildings. Injury to the spleen was the most frequent form of visceral damage to occasion a fatal issue; but the liver, kidney, duodenum, and small bowel were also damaged in mortal injuries, and in 1 case hemorrhage from the uterine vessels caused a fatal hemoperitoneum.

In casualties due to air bombardment of cities, many of the injuries are not the primary effects of the explosion, i.e., are not produced by splinters or the direct impact of a blast wave. Perhaps most casualties are due to the secondary and tertiary effects of the bomb detonation.

Those effects are said to be secondary when injuries are due to the patient being bowled over by the blast wave or as a result of a splinter wound and thus injuring himself (Zuckerman). Tertiary effects are due to the impact of dislodged masonry, fragments of wood, or other missiles, the collapse of shelters, houses, etc. Quaternary effects may also be encountered, in which injury or death is due to asphyxia following burial under débris, carbon monoxide poisoning, etc.

The rôle played by blast in determining fatal abdominal casualties is certainly not a large one.

The following cases illustrate the various causal mechanisms operating in cases of subparietal abdominal injury met with in this war.

A patient, a woman of 43 years, was blown by blast across a room against a steel partition; the building then collapsed on her, crushing her shoulder down into a crouching position. Release was effected in about half an hour after the "incident." Contusion of the lung, possibly due to blast, was diagnosed. In view of the thoracic condition, the abdomen was most wisely opened *under local anesthesia*. The pelvic hematoma was found to have stripped the peritoneum half way up the abdomen. The anterior wall of the bladder was greatly bruised; suprapubic drainage was instituted; pure blood had previously been obtained on catheterization. Convalescence was complicated by consolidation of the left lung, paralytic ileus, and by temporary insanity. Ultimately, recovery was complete (Miss Louden's case).

The abdomen of another patient has been severely contused by flying bricks from a direct hit by a bomb on a street air raid shelter; one man had 2 perforations of the jejunum, which were successfully sutured; a hematoma of the mesentery was also evacuated.

Under similar circumstances, a woman had an ovarian cyst ruptured; 4 pints of blood-stained fluid were evacuated from the abdominal cavity and the sac of the torn tumor was removed. Recovery took place.

The collapse of the roof of a house which had received a direct hit produced a complete division of the jejunum in a man of 62, who recovered after an end-to-end suture of the bowel.

A crush injury due to collapse of a wall produced a separation of the pubic bones at the symphysis, and a fracture of the ilium posteriorly, but had also torn the mesentery of the terminal small gut; the laceration was transverse, and two arteries were still spurting at the time of operation; the bowel was viable. The man made a good recovery.

Winifred C., aged 28 years, was admitted to hospital for injuries sustained when her house collapsed upon her, and a piece of concrete fell across her abdomen. Her injuries included multiple abrasions on the face, 3 deep wounds of the scalp extending down to the bone, a deep wound of the medial aspect of the left knee which did not implicate the joint, and a wound over the left olecranon. An indefinite resistance was found in the right iliac fossa, some tenderness in the epigastrium was complained of, and resistance was demonstrable in that area. A pseudopancreatic cyst finally developed in the left portion of the lesser peritoneal sac; an extensive retroperitoneal extravasation was found which had mainly spread towards the left and downward along the descending colon. The cyst was successfully drained.

Other nonpenetrating abdominal injuries have been received as a result of the detona-

tion of mines at sea; the exact mechanism has not always been evident; in some cases decks have actually fallen in and exerted a crushing effect.

A man was admitted from a "mined" ship; the galley in which he worked caved in upon him. In addition to burns of both hands, he had a diastasis of the symphysis pubis, and a fracture of ascending and descending pubic rami. A small extraperitoneal rupture of the bladder was present, and there was urinary extravasation into the Cave of Retzius. Postoperative ileus complicated his convalescence, but he ultimately made a good recovery (Mr. W. E. C. Wynne's case).

Another man admitted from a mined ship had a fracture dislocation of the knee and evidence of abdominal injury. He had been in the water some time before being picked up. There was gross bruising of the transverse mesocolon, and also numerous petechiae on the bowel wall. The right kidney was contused. The limb required amputation, but the man recovered (Mr. W. E. C. Wynne's case).

Some abdominal injuries have definitely appeared to have been caused by blast. Mr. D. H. Patey had 1 case, in which a man running away from a bomb was exposed to the blast wave. There was no sign of any external injury and no history of any blow from any fragment of timber or masonry. His mesocolon was torn in the vicinity of the splenic flexure of the colon with resultant hemorrhage.

Another case was that of an intramural thrombosis of the blood vessels of the right side of colon. (Mr. Blacon Yates' case.)

P. H., male, aged 38 years, was admitted to hospital in a state of extreme shock; he had been in close proximity to a detonating bomb, although the exact distance which separated him from the missile was never actually determined. Abdominal pain was not marked; 1,000 cubic centimeters of plasma was first administered by drip transfusion, then a pint of blood, followed by 600 cubic centimeters of 5 per cent glucose saline. His general condition slowly improved; 24 hours after admission the abdominal pain became more severe, especially on the left side of the abdomen. At 30 hours, clinical evidence of diffuse peritonitis was apparent, and laparotomy was performed. The only visceral lesion discovered was gangrene of the anterior surface of the cecum and proximal 2 inches of the ascending colon. The condition appeared to be due to intramural thrombosis of the vessels of the bowel wall; the vessels of the mesentery were quite normal.

W. J. L., under the care of Mr. H. Donovan, succumbed from subparietal injury; this case definitely appears to be one of blast injury to the abdomen. The thoracic pathological findings confirmed the nature of the causative mechanism; the liver showed intrahepatic tears and hemorrhage, and a large subcapsular hematoma. The right suprarenal also contained a hematoma. The inferior pole of the cecum contained a small hematoma; the ascending and transverse colon exhibited marked bruising. There was a tear in the seromuscular tunics of the transverse colon.

In Mr. Hamilton Barclay's case, a man was in the open when a high explosive bomb detonated in close proximity to him. He had not been struck by any fragment, nor fallen on his belly. There was a large hematoma of the great omentum, and a certain degree of hemoperitoneum. An extensive retroperitoneal hematoma was present, and a horizontal rupture of the abdominal wall, the tear extending from the peritoneum through the muscular wall of the parietes to the skin, which was intact.

In respect to injuries due to blast, it must be remembered that "blast injury of the lungs" by reason of the abdominal pain produced may suggest the diagnosis of an abdominal lesion. Some of these patients have rigid abdominal walls; possibly the pain and rigidity may be caused by hemorrhage in the thoracic intercostal spaces.

X-ray examination of the chest should enable a diagnosis to be made of pulmonary concussion, and the physical signs in the chest, especially the bulging of the chest wall, should prevent an unnecessary laparotomy.

Nonpenetrating or subparietal injuries of the abdominal viscera may occur under circumstances less directly connected with the destructive mechanisms and missiles of total warfare. The "black-out" is a fruitful source of such mishaps, their name is legion and their variety infinite.

The subject of "*Immersion Blast*" is being dealt with by Surgeon-Commander Rex Williams R.N. in his Hunterian Lecture in 1942, and also by the writer in his Bradshaw Lecture for 1942.

Lesions of the stomach in "total" warfare. This war has added little to our knowledge of penetrating wounds of the stomach. Operations for wounds of the stomach have given a recovery rate of 60 per cent in this series from the present war; this is a marked advance from 36.3 per cent in the last war (Cuthbert Wallace). Wounds are of infinite

variety, depending on the size, shape, and velocity of the missile, the direction of its flight, the state of the stomach in respect to repletion or vacuity, etc. In some cases, the wounds have been wide and gaping; in a wounded man coming under the care of Mr. Blacow Yates the wound in the stomach was 4 inches long, and the mucous membrane was extensively everted; in another patient, operated upon by Surgeon Lieutenant-Commander B. C. Murless, R.N.V.R., the gastric rent extended from the esophageal opening to the greater curvature. In a successful case of Mr. J. Scholefield, the stomach wound was 3 inches long.

Eversion of the inner tunics of the stomach wall was said in the last war to be most marked at the curvatures and in wounds of considerable dimensions. In the present series of cases under review no mention is made of the "note of exclamation" wound, to which Sir Cuthbert Wallace drew attention. In several of the recent cases, severe hemorrhage has taken place into the celomic cavity.

There is one condition of the stomach which has impressed by the striking frequency of its occurrence in this war—*acute dilatation of the stomach.* Not only has this phenomenon been a concomitant of penetrating injury of the abdomen, but it has also proved an undesirable and sometimes intractable sequel of operations undertaken to repair the damage inflicted by the detonation of bombs from enemy aircraft.

H. H., male, aged 35 years, was injured by bomb fragments; there were multiple flesh wounds of left thigh, buttocks, and epigastrium. An exploratory laparotomy revealed no visceral injury; the patient had to be prematurely evacuated to a base hospital, where he arrived very ill and shocked and was found to be suffering from acute dilatation of the stomach. This was relieved by continuous suction drainage; intravenous infusion promoted a satisfactory convalescence.

A girl of 17 was in the kitchen of a house which received a direct hit from a bomb; the house came down on top of her father (who died shortly after admission to Hospital), her mother and two day old baby (who both recovered) and herself. She was moderately shocked; extensive bruising of the pubic region and chest was present. Radiography showed fractures of the ischium and pubes on the right side and of both rami of the pubis on the left side. The radiologist commented upon the condition of acute dilatation of the stomach. At operation, an extraperitoneal rupture of the urinary bladder was found. Despite suction drainage of the stomach, the gastric condition never ameliorated, and she succumbed 96 hours after operation.

Surgeon-Commander Rex Williams, R.N., in private communication, mentions a case of penetrating wound of the abdomen that died on the sixth day from acute dilatation of the stomach, despite every effort to control the complication.

Acute dilatation of the stomach may supervene at a still later date after wounding, may defy all treatment, and may determine a fatal ending.

A patient was admitted to hospital for injuries from a bomb explosion occurring a few minutes before. Shock was profound; the patient was very pale, cold, clammy, apathetic, but not restless. There was a gross compound fracture of the upper third of the left femur, and there were "sucking" entry and exit wounds of the right chest. After a period of resuscitation lasting 4 hours, during which 4½ pints of blood were administered, the patient's injuries were dealt with simultaneously by two surgeons. Mr. Kilpatrick performed a débridement of the thigh wound, and the limb was placed on a Thomas's splint with skeletal traction. The abdominothoracic injury was admirably treated by Mr. Wass. There was no wound of the lung, but a wound in the diaphragm and liver. He was evacuated to a base hospital 9 days after his injury. Six days after his admission to base hospital he became very ill: temperature, 100 degrees; pulse, 120–130; the chest condition was considered satisfactory. He had been vomiting bile stained material for the previous 2 days, but there was no clinical evidence of a dilated stomach. A stomach tube was introduced and left *in situ;* despite this, vomiting persisted, and he died 16 days after he was wounded. The postmortem revealed the presence of an *acute dilatation of the stomach;* a few cubic centimeters of blood were present between the liver and diaphragm. The chest wound was healed, and the state of lungs and pleura was considered satisfactory.

Mr. N. R. Barrett and Mr. Price-Thomas have drawn by attention to the *sudden acute dilatation of the stomach* which *frequently* takes *place in contusions of the chest.*

Perforation of peptic ulcer. The circumstances under which perforation of a peptic ulcer may occur and operation be undertaken for its repair may invest a mundane occurrence and a banal surgical procedure with a dramatic color.

Several ulcers are known to have perforated during air raids on the country and several have been operated upon during the "blitz":

A male patient, T. D., perforated a duodenal ulcer during progress of an air raid on Merseyside and was removed to Hospital; operation for its repair was in progress, when the hospital got a direct hit, putting the operating theater department completely out of action. The laparotomy wound was temporarily closed, the patient removed to another institution, where the operation was completed by the resident surgical officer; the man recovered.

Another patient was being operated upon for a perforated duodenal ulcer when the detonation of a mine in close proximity brought the roof of the theater with superjacent sandbags down upon patient and those engaged in the operative relief of his condition. The emergency lighting system fortunately proved itself worthy of its name, and the operation could be continued. The débris, glass, dust, and sand were assiduously removed from the abdominal cavity; the perforation was sutured. The man made a good recovery, his only complaint being of "the dust in his eyes."

A rear-gunner in a Blenheim bomber perforated a duodenal ulcer over Dunkirk; he thought that he had been wounded by "Flak."[1] On the return of the aircraft he was admitted to hospital as a casualty from enemy action; no wound was discoverable. The real condition was then diagnosed, and the patient successfully operated upon by Group Captain Stanford Cade.

I have knowledge of at least 3 ulcers which perforated during the "Dunkirk miracle," in which recovery took place. The number of loyal stout-hearted men who, weary though they were, contributed in diverse fashions to the ultimate recovery of their comrades cannot have been inconsiderable.

Intestinal injuries. The recovery rate of intestinal injuries due to enemy action which are operable has surprised me. Of the patients with small bowel lesions 47 per cent have recovered; and 40 per cent of those with large gut lacerations. Suture carries a lower mortality than resection for wounds of the small intestine and should be preferred whenever possible. This doctrine, as the perusal of case records clearly demonstrates, is firmly inculcated in the minds of British surgeons; in the Spanish War operators seemed disposed to resect when the ileum was the segment of bowel damaged and to suture when the jejunum was involved. The type of resection and anastomosis employed is a matter of individual choice and experience, and is not a fashion which varies from war to war. My predilection led me to use end-to-end suture in the last war in every intestinal injury in which bowel resection was indicated.

The specter of the "dangerous mesenteric angle" was permanently robbed of its terrors in the light of the experience of the last war, since no case was found to demonstrate that fatal peritonitis was ever due to leakage at that angle. Peritonitis was invariably due to infection introduced with the missile at the time of wounding or subsequently from the injured gastrointestinal tract, especially the large gut, and was in no way causally related to the technique of bowel anastomosis. Lengthy resections of small intestine imply severe and widespread wounding; the ablation of short segments of gut is therefore more promising. Nevertheless, the removal of 6 feet of small intestine and the cobbling of other injuries proved successful in the last war (Owen Richards, Gordon Bell, Gordon-Taylor); in this war Surgeon Commander T. N. D'Arcy, R.N., saved a 6-foot resection of small bowel severely damaged and burned by a phosphorus bullet; F. H. Bentley, a 4-foot resection.

I have sometimes been credited with the advocacy of resection as opposed to suture in cases of injuries to the colon produced by enemy action. This is far removed from the truth. There can be no doubt about the place of suture in most intraperitoneal colon wounds, and also about the indication for suture in conjunction with efficient drainage of the neighboring area in many extraperitoneal injuries when this technique offers a reasonable prospect of success; suture, local chemotherapy, and drainage of the damaged area may be combined with proximal colostomy in cases in which grave infection is feared.

Colostomy sometimes proved valuable in the last great war as a prophylactic measure against infection of the lethal retroperitoneal tissues; if this operation is performed, it should be practiced early, before infection has secured a firm hold of the region. Sulfonamide therapy, local and oral, has already proved a valuable adjuvant to surgery for patients with damaged large intestine, and its routine use prophylac-

[1] A fragment of anti-aircraft shell.

tically is to be recommended. I foresee nothing likely to alter the indications for resection of the injured colon which I have ventured to promulgate on more than one occasion: (a) the cecum or colon is in a state of infarction; (b) there is extensive separation of the bowel from its mesocolon or vascular supply, especially if the mesocolon is also the site of a hematoma or is actively bleeding; (c) the vitality of the bowel is extinguished by a large piece of metal or other fragment hurled with the cyclopean force of modern high explosive; (d) the wound of the large intestine is of such magnitude, or the surgical approach to the part of the colon damaged is associated with such difficulty, as to suggest the formation of an artificial anus as a surgical *pis aller*.

I only know of two successful exteriorization operations for injuries of the large bowel in this war.

In the traumatic colonic lesions of war it is preferable to complete the resection quickly by the form of anastomosis with which the operator is most familiar. The addition of a prophylactic or of a temporary intraperitoneal colostomy is a useful and perhaps life-saving expedient.

Multiple resections of bowel. Multiple resections of bowel were often successfully performed by surgeons before the last war for various pathological conditions unconnected with traumatism. During the war of 1914–1918 plurisegmental resections for injury aroused grave forebodings in the minds of operators, and various recommendations were made in order to obviate the necessity of removing more than one length of damaged intestine. Nevertheless, I had 11 successful cases of double resection, which represented a 50 per cent recovery rate in the patients submitted to this operation at my hands. No case of a successful triple resection for gunshot injury of the bowel was known to me in the last war, although W. A. Campbell had a triple resection with death from a chest complication when success appeared to be within his grasp. During the last 25 years successful multiple resections of intestine are of almost everyday occurrence, and I myself have had numberless cases of double and even of triple ablations. I recall the case of 1 patient who actually survived the removal of 7 segments of bowel for a complex and complicated carcinoma of the colon!

During the present War, Meyrick Thomas has brilliantly and successfully performed a quadruple resection of small intestine damaged by a "tommy-gun" at close range:

T. L. was shot in the abdomen at short range, about 2½ hours previous to admission to hospital. There was a small wound of entry about 1 inch below the umbilicus, with about 2 inches of bleeding omentum protruding. At operation, apart from several simple sutures of damaged gut, 4 resections of shredded length of ileum about 1 to 2 inches long were found necessary; end-to-end union was employed in each case. The distance separating the various anastomoses varied from 12 to 18 inches. Four wounds of the bladder were found, but the condition of the patient did not permit of anything more than a temporary suprapubic drain. He made a good recovery.

Protrusion of the abdominal viscera. Prolapse of the omentum has a diagnostic rather than a prognostic value; the prognosis depends upon the associated visceral damage rather than upon the fact of damage or extrusion of the omentum itself.

Hernia of the bowel resulting from enemy action varies from complete evisceration to the protrusion of one or two segments of intestine. Over 20 years ago cases with extrusion of gut were accounted "bad surgical risks"; nevertheless, Owen Richards' successful pioneer operation was performed upon a soldier with extruded and damaged intestine. Among others, the writer had several successful cases of suture or resection of prolapsed bowel. From the material now under review, the *recovery rate from operation for prolapsed and nonperforated small intestine* is about 50 per cent, the mortality being mainly determined by concomitant damage; but *when the small gut is not only extruded but also injured*, the mortality is about 80 per cent.

In cases of *prolapse of the large bowel*, the prognosis is very grave, although several remarkable recoveries have been effected by skillful and courageous surgery. For example, Mr. F. J. S. Heaney successfully operated upon a man of 26, who was injured in the street by a bomb splinter. On his admission to hospital the large intestine extruding feces was found to be prolapsed through a large rent in

the left loin. After resuscitation with 2 pints of plasma, he was operated upon 3 hours after admission.

The wound was thoroughly excised, the damaged prolapsed descending colon was removed, and a side-to-side junction effected between the transverse and the pelvic colon. The peritoneum was completely closed, but the posterior portion of the flank incision was left open. A prophylactic temporary cecostomy was performed. A fairly normal convalescence was established.

In view of the grave prognosis which attends *prolapsed and damaged bowel*, the following cases are noteworthy.

A patient (Mr. O. V. Lloyd-Davies' case) was admitted to hospital with a huge lacerated wound of the lower right quadrant of the anterior abdominal wall, and most of his bowel lying in his trousers. Shock was profound, but the man was conscious. The usual methods of resuscitation were utilized, including a blood transfusion; the clothing was slit up, and the prolapsed bowel merely covered with a warm saline pack. The abdomen and the extruded gut were covered with stone fragments, mud, mortar, etc.; the 2 lacerations of the ileum were repaired by suture. The wound in the abdominal wall was widely excised; the extent of tissue loss was now alarmingly evident, and much ingenuity was required to close the peritoneal and muscular gap. The skill of the surgeon and the scientific postoperative measures contributed to the successful issue. (a) Continuous stomach suction was continued until normal peristalsis was heard all over, and until there was no distention and the bowels were open normally. (b) Continuous intravenous drip (1 bottle of normal saline in proportion to 4 bottles of isotonic glucose; if good cloud of urinary chlorides, glucose increased and vice versa). This was continued for 13 days. As much as 15 pints per 24 hours had to be given at first to keep pace with the measured and estimated fluid loss. Peristalsis gradually became normal, low-pitched and present all over the abdomen; fluid was now passing through from the stomach; careful dosage of prostigmine, 1 cubic centimeter intravenously, and later small doses of Epsom salts started normal bowel action. The wound was septic, but held together astonishingly. Three months later the man was readmitted to hospital with signs of intestinal obstruction. A straight x-ray picture showed numerous small gut fluid levels all over the abdomen. At operation, numerous adhesions were found, most marked in connection with the lower small intestine and in the ileocecal region. Multiple adhesions were divided; a small perforation occurred and was sutured. After-treatment was the same as before. Recovery was complete and he is doing moderately heavy work, wearing a canvas belt.

A member of a bomb disposal squad (Mr. Geoffrey Parker's case) was standing in the open, about 10 yards away from the bomb, when it exploded. His clothes were partly torn off, and his intestines were found "lying in the grass." On admission to hospital, he had a large wound in the right iliac fossa, about 4 inches diameter in all directions. A field dressing somewhat inadequately covered the 3 feet of prolapsed ileum. One loop of ileum had 2 large rents, almost completely dividing the bowel; the mesentery of this portion of the bowel was also damaged. A limited resection of small gut was performed. The parietal peritoneum was also extensively torn up, and blood had exposed the extraperitoneal aspect of the bladder, and had tracked through the femoral canal into the thigh and along the spermatic cord. The blood was found to come from the horizontal ramus of the pubis, in which was impaled a small piece of bomb casing. The man made a good recovery.

Wounds of the duodenum. The Spanish War confirmed the sinister reputation of wounds of the duodenum and pancreas which had been established in the great war of 1914–1918. The number of cases of injury to the duodenum at present available is too small for any reliable conclusions to be drawn as to the fatality of these wounds; it may be said, however, that successful operations have been performed for duodenal injuries in this present war (Rex Williams, Hedley Atkins, Henry R. Thompson and T. J. Cobbe).

Driver B. (Mr. Hedley Atkins' case) was wounded in the loin by a machine gun bullet while lying face downwards on the deck of one of H. M. Destroyers which was transporting him from Dunkirk to England. The wound of entry was about half an inch in diameter and situated close to the spine; the track thence passed forwards and to the right between the first and second lumbar transverse processes. When seen 4 hours after wounding, his general condition was good. He had vomited once or twice; his upper abdomen was rigid, but peristaltic sounds were normal. The wound in the loin was first dealt with, and next the abdomen was opened by a high right paramedian incision. The peritoneal cavity was full of blood; there was a perforation of the anterior wall of the second part of the duodenum, and also on the posterior surface of the liver; from this latter blood was oozing freely. The bullet had obviously skirted the medial border of the superior pole of the right kidney and had damaged both walls of the duodenum. The wound of the anterior wall of the duodenum was sutured; the peritoneal cavity cleared of blood by suction, and the rent in the liver plugged with gauze. Some discharge of duodenal contents took place from the wound in the loin, but this ceased after a few days and the man made a good recovery.

Rare as are successful operations for duodenal injuries, Henry R. Thompson has actually two to his credit:

Jack S., a boy of 16, was hit in the street by a fragment of bomb. On admission to hospital, shock was severe; there was cyanosis of lips and cheeks. He complained of pain "in the pit of the stomach," and had vomited once. There was retrograde amnesia. A puncture wound was present, 1 centimeter in diameter and situated 1½ inches internal to and just above the left anterior superior iliac spine. There was marked tenderness over the ascending colon, and an absence of intestinal sounds. There was a graze over the right costal margin, and a small wound on the flexor aspect of the left forearm. At operation a perforation of the duodenum near the pyloroduodenal junction was closed by suture; and a similar perforation of the anterior wall of the stomach was treated in a similar fashion. Despite a subsequent right basal pneumonia, the patient made a good recovery. A fragment of metal was seen on x-ray examination to be still present in the right upper abdominal quadrant, probably in the liver.

The second, a man, sleeping in bed on his back when, as a result of a "near miss" bomb, was awakened in the small hours of the morning by what appeared to be a severe blow on the abdomen; the injury may have been due to "blast," or some fragment of the house may have hit his abdomen, although there was no bruise or abrasion to indicate such a mechanism. On admission to hospital, the patient was in considerable abdominal pain; the pulse rate was 80; he was tender and rigid in the upper right abdominal quadrant. The man was kept under close observation, and after 3 hours, although there was no change in the pulse rate or in its volume, the tenderness and rigidity now involved the whole of the right side of the abdomen. Operation was performed 6 hours after the injury. A large subserous hematoma was found, which had spread over the duodenum from the pyloric end of the stomach and had infiltrated into the layers of the transverse mesocolon. The peritoneum over the duodenum was found to be ruptured at the junction of the first and second portions. The rupture of the bowel was not quite complete; about ½ centimeter gut wall was still intact. At the site of the tear the various coats of the bowel had been separated and stripped asunder; the prospects of a satisfactory end-to-end junction seemed doubtful. Accordingly the duodenum was completely divided; the two ends were closed, and a posterior isoperistaltic gastrojejunostomy was performed. The man made a good recovery.

Surgeon-Commander Rex Williams performed a successful operation in the case of a laceration of duodenum:

W. B. Bracey, aged 24, seaman, was admitted from sea with a penetrating wound of the right flank which resulted from an enemy bombing attack.

TABLE I.—RECOVERY RATE OF INTESTINAL INJURIES

Injuries of the small intestine	
Total number undergoing operation for injuries including small intestine	253*
Number of recoveries	121
Percentage of recoveries	47.3†
Number of operations for abdominal injury confined to small intestine	119
Number of recoveries	75
Percentage of recoveries	64
Injuries of the large intestine	
Total number undergoing operation for injuries confined to large intestine	163‡
Number of recoveries	65
Percentage of recoveries	40§

*Represents 43% of all operations for abdominal injuries; Sir Cuthbert Wallace reported 30% in 1918.

†Sir Cuthbert Wallace reported 37.5% in 1918.

‡Represents 27% of all operations for abdominal injuries.

§Sir Cuthbert Wallace reported 42% in 1918.

Severe shock was present and was promptly treated. After an interval of approximately 12 hours after the receipt of injury, the abdomen was opened through a right upper paramedian incision. The second portion of the duodenum was found to be almost completely torn across, and there were also penetrating wounds of the proximal jejunum and transverse colon. The duodenum was sutured in its transverse axis and the other injuries repaired in similar fashion. No foreign body was found; 10,000 units of Bacillus welchii serum were introduced into the peritoneal cavity and the abdomen closed with 1 drainage tube. Recovery was uneventful. When he was seen 2 months later, he had returned to duty, and a barium meal investigation revealed no abnormality in the stomach, which was empty in 4½ hours. The duodenal cap filled well, appeared normal, and was not tender. A large metal fragment was seen in the abdomen lying posteriorly, behind the pyloric portion of the stomach.

Yet another case of a wound of the duodenum successfully treated is that of Mr. T. J. Cobbe:

The patient, C. M. M., a mate, recovered from injuries due to a fragment of bomb which not only damaged both walls of the stomach, but also wounded the duodenum and the colon.

Injuries of gall bladder and extrahepatic biliary tract. In this series there seems to be only 1 case of injury to the gall bladder. This was successfully dealt with by Miss E. M. Hall, F.R.C.S. There were multiple injuries including a penetrating wound of the abdomen; a perforated gall bladder and a ruptured liver were found at operation. The liver was sutured and the gall bladder was drained. There were

many other injuries affecting the skull, eyes, forearm, hand, etc.; nevertheless, the patient recovered.

Injury to biliary tract due to "blast." Kathleen T., aged 3 years, was the only survivor in a few houses which were completely destroyed by high explosives. She was the only living being when rescue parties arrived at the scene of the "incident." On admission to hospital she was in a state of severe shock. Apart from slight bruising of the right shoulder, there were no lacerations or external injuries. The abdomen was rigid and tender. After several hours the respirations became more rapid, and vomiting occurred. Operation was beyond consideration; a diagnosis of a ruptured diaphragm was tentatively put forward by me. After about 5 days the general condition slowly improved; the function of her bowel was restored; vomiting much less frequent. In 3 weeks' time the abdomen was becoming more and more distended in this lower portion, and its increasing size embarrassing both eating and movement. Twenty-five days after the "incident" the abdomen was opened under gas and oxygen; a large cystic swelling filling the whole abdomen was found, whose upper limit was not determined. Eight pints of bile-colored fluid were evacuated, and reported upon as consisting of "bile remnants." From this time her recovery was almost uneventful, and she is now well (Mr. J. H. Buttery's case).

Injuries of the spleen. The spleen has proved very vulnerable in this war, and has been damaged by penetrating injury, by subparietal crushes and by the effects of "blast." In such fatal nonpenetrating injuries from crushing mechanisms, burial, etc., as have come to autopsy, the spleen has been the organ most frequently damaged, when death has been solely or chiefly attributable to the abdominal lesion.

The recovery rate has been 55 per cent, which is a 10 per cent improvement on the figures of 1918.

Injuries of the appendix vermiformis. In only 2 cases in this series collected from this war has there been any note of an injury to the appendix. In 1 case, the injury was inflicted by a revolver bullet; in addition, there were 4 wounds of the terminal ileum. The man recovered.

Injuries of the rectum. In this present series, 52 per cent of patients with injuries of rectum have lived, an improvement on the 33 per cent recovery rate in the last great war (Sir Cuthbert Wallace). When the bladder is injured as well, 33 per cent recover.

Several cases have been observed of the explosive wound of the perineum; this seems to occur when the missile passes superficially across it. The sphincter surrounded by a circumanal ring of skin may be torn away from the surrounding skin, and may be drawn high up into the perineal tear. Mr. W. B. Gabriel and Lieut. Col. Cameron MacLeod, R.A.M.C. have observed such a case in this war.

The value of the local employment of sulfanilamide powder in rectal injuries seems to have been clearly demonstrated in the successful case of a patient operated upon by Surgeon Commander Frank Stabler, R.N.V.R.

A Nazi officer in an E-boat was admitted to hospital with wounds in the back and buttocks from fragments of a shell from one of H. M. Destroyers. One of these splinters traversed the sacrum and damaged the underlying rectum. This posterior wound was excised, damaged fragments of sacrum were removed, and powdered sulfanilamide was insufflated in the track. Laparotomy was then performed, and a perforation of the rectosigmoid junction was sutured. A retroperitoneal hematoma was evacuated. No colostomy was performed. This type of case with bone injury, presacral blood extravasation and an associated large bowel injury did extremely badly in the last great war; the use of the sulfonamides marks a definite advance in the treatment of this type of case.

Injuries of bladder. Penetrating wounds of the bladder have shown a recovery rate of only 35 per cent, which is rather lower than the 40 per cent of the last war (Sir Cuthbert Wallace). The recovery rate is approximately the same when the bladder is injured along with the rectum or colon.

The reminder to examine the interior of the bladder digitally, when there is perforation of that viscus, will often lead to the discovery of the missile. A bullet was even found lodged in the prostatic urethra (Major A. S. Till, R. A. M. C.).

Complicated abdominal injuries. Multiple wounds of the abdominal viscera, especially the hollow viscera, manifestly render the prognosis of injuries to the belly more grave. The factor of serious concomitant hemorrhage makes the outlook still more serious.

A man was hit by a machine gun bullet. There was a small wound of entrance in left epigastrium over the left rectus at the level of the uppermost linea transversa; blood and air were bubbling out of this wound. Small wound of exit through left erector spinae, the level of which was about 1 inch lower than the en-

trance wound. This wound was very small, bled very little, and was situated just lateral to the transverse processes. Lesions found at laparotomy included: (1) perforating wound of anterior surface of stomach, close to greater curvature with severe bleeding from this perforation, about ½ inch in diameter; (2) posterior surface of stomach, wound of exit into lesser sac with very little extravasation; (3) perforation anterior surface of terminal part of duodenum close to duodenojejunal junction; there was severe bleeding from this wound; (4) perforation of posterior surface of duodenum, but comparatively little extravasation; (5) severe bleeding from transverse mesocolon (right colic vessels); (6) large bowel in condition of spasm, small bowel dilated and immobile. The case ended fatally.

Two wounded patients were admitted simultaneously to the same hospital, an old woman of 78 years and a girl of 3 years. Age perhaps did not play such an important part in determining the fatal ending, for in each case the injuries were of multiple or severe character. In the case of the old lady (Mr. H. R. S. Harley's case) there were present: (1) laceration of upper and outer part of the right thigh involving the deep fascia; (2) compound fracture of the trochanteric region of the left femur, with retained foreign body; (3) 6 lacerations of the buttock; (4) Pott's fracture of the left ankle; (5) laceration of scalp; (6) tender, rigid abdomen in which autopsy revealed much blood, and 2 large perforations of the jejunum. A retained fragment ½ by ½ inch was present.

The child of 3 years was admitted a quarter of an hour after the "incident" in a condition of extreme shock. A single wound covered with brick dust was present, and from it there protruded several feet of dust covered small intestine. After intensive resuscitation, the small intestine was washed and replaced inside the abdomen by Mr. Wass in an incredibly brief space of time. Despite every measure, death ensued.

An officer, at the termination of a parachute descent, landed in the fork of a tree, and received a penetrating wound of the rectum, a branch disrupting the pararectal tissues right up into the iliac fossa; the peritoneum was untorn. The injured man then fell to the ground, sustaining a severe fracture of the pelvic girdle. There was a wide separation of the symphysis, and a disruption of the sacroiliac synchondrosis. He survived his injuries about a year.

On the other hand, some cases have made splendid recoveries:

R. H. R., male, was injured by a splinter of bomb and sustained damage to stomach, transverse colon, and small intestine. There were also injuries to the right kidney, left leg, and left arm. The wounds of the stomach and small bowel were sutured. The colon was so severely damaged that a resection of a piece of the large bowel was necessary. Recovery (Case of Mrs. G. M. B. Toland, F.R.C.S.).

C. W., male, aged 34 years, was admitted to hospital half an hour after the "incident." He was found to be suffering from the following injuries: (1) penetrating wound over the middle of the upper part of the right rectus abdominis. Examination of the abdomen demonstrated rigidity and generalized tenderness; (2) a through-and-through wound of the middle of the left thigh with a retained foreign body but no bone injury; (3) penetrating wound of the left leg with a retained foreign body; (4) superficial laceration of the buttock. Operation took place 6½ hours after injury; 2 surgeons (Mr. Wass and Mr. Thomas) co-operated. Three pints of blood were found in the peritoneal cavity. There was a wound of the greater curvature of the stomach, near the pylorus, a wound of the transverse colon and 7 wounds of the small bowel, from one of which a bomb fragment was removed. All these perforations were sutured. A rent on the inferior border of the liver, which was not bleeding, was left alone. Recovery took place.

A sailor with almost every region of his body damaged, including his small intestine, was successfully operated upon by Surgeon-Commander Frank Stabler, R.N.V.R.

The man was hit by cannon shell 16 hours before admission to a naval hospital. He had the following injuries: (1) frontal region laceration with fracture of outer table of skull; (2) 2 punctured wounds of abdomen above pubis, which had produced 6 perforations of jejunum about 2 feet from duodenojejunal flexure; (3) right hand, index and middle fingers blown off, fifth metacarpal compound fracture and many penetrating wounds; (4) compound fracture of left olecranon; (5) 9 punctured wounds of left thigh; (6) 1 punctured wound right thigh; (7) compound fracture of left patella. Seven inches of bowel were excised, including 5 perforations; the sixth perforation was treated by separate suture. No drainage was employed. In the space of 12 hours, 11 pints of blood and plasma were given.

An associated severe fracture, especially a compound fracture, loads the scales heavily against the victim with an abdominal injury; a smashed femur complicating a belly wound or contusion, especially at its upper extremity, is a burden hardly to be borne by suffering humanity.

Nevertheless, such patients have survived:

Mr. Kenneth Bond had under his care a bomb injury admitted with a small opening close to the anus, which led into a large cavity on the right side of the rectum and involved a complete division of all the sphincters, including the anorectal ring. The man had also sustained multiple fractures of the anterior portion of the pelvic ring, and an incomplete rupture of the urethra. Finally, a double spiral

fracture of the right femur completed the list of his injuries. The end-result consisted in a complete recovery of function of all the systems involved.

A patient of Mr. F. G. Wrigley actually survived an *injury to the abdomen and a compound fracture of both femora:*

This patient (Mr. F. G. Wrigley's case) received a bomb injury to abdomen, with contusion of colon, damage to omentum, extensive extraperitoneal wound of lower left iliac region, bilateral compound fracture of femur, wounds of right forearm, and right temporal region. She recovered from the abdominal injury, although a fecal fistula formed 4 months later. She ultimately succumbed from mental deterioration and the effects of sepsis in connection with one of the wounds of the thigh.

In a patient who was under the care of Mr. A. L. Candler, after she had received a *penetrating wound of the abdomen and a fracture of the right femur*, a completely successful result was obtained.

This occurred in a woman of 30 who was putting out incendiaries on the night of an intense raid on a city. On admission to hospital, shock was extreme. After measures for resuscitation had been employed, laparotomy was performed, and several intestinal perforations sutured. The hospital was badly damaged the night following, and the woman was transferred to an infirmary in another town; her pulse was 120 after her transportation. Her subsequent course was punctuated by several alarming or disquieting incidents; large quantities of pus and blood were passed by the rectum, and a transfusion of 3 pints of blood on one occasion was required. A few days after this a small intestine fistula appeared at the bottom of an unhealthy-looking abdominal wound. This finally healed, the patient making a complete recovery.

An unusual mode of wounding was noted in the case of R. A. C. who was blown by the blast wave from a detonating bomb on to the roof of the car beside which he was standing. Then came a second bomb, from which he received 16 superficial splinter wounds of the left lower limb, but also a penetrating injury of the belly. No visceral injury was discovered on laparotomy. The man recovered.

It is possible for those persons who are *maimed by high explosive*, in addition, to *suffer from burns.*

H. W. W., male, aged 46 years, was extinguishing an incendiary bomb with sand when it exploded. He received burns of the face and hands, and 4 punctured wounds of the abdomen. At operation, 1 large and 1 small wound of the ileum were sutured, as well as a small tear of the transverse colon. He recovered.

ABDOMINOTHORACIC INJURIES

Uninformed lay opinion is prone to associate penetrating injuries of the trunk with a dire mortality, and statistical inquiry only too truly confirms the fatality of wounds involving certain lethal anatomical areas, and the severity or serious consequence of many wounds of the less mortal regions of the thoracico-abdominal zone under conditions of modern warfare. The behavior of wounds of the diaphragm itself had been known to surgeons since the days of Ambroise Paré, and was accurately noted and discussed by Guthrie when writing of the war surgery of the Napoleonic era. The operative treatment of thoracic wounds by Guthrie and by Baron Larrey, Napoleon's great Surgeon General, anticipated, though in immature fashion, the modern treatment of wounds of the chest received under conditions of war. The early story of the abdominal aspect of the problem has already been told.

Injuries which involve thorax, diaphragm, and abdomen may be of penetrating or of non-penetrating character. In the war of 1914–1918, the first named group completely overshadowed and outnumbered those which were subparietal lesions; in this present conflict the cases for which surgery is possible still belong almost exclusively to the former class.

Penetrating injuries. In one series of cases from the war of 1914–1918 (Sir Cuthbert Wallace, 1922) abdominothoracic cases constituted 12 per cent of the abdominal cases which reached the casualty hospitals of one army; the operations performed on this group of patients also accounted for 12 per cent of all the abdominal operations in that army. In the Spanish Civil War the percentage of the bellies admitted to a hospital of first urgency was not dissimilar to that which obtained in 1914–1918, i.e., 11 per cent (Jolly, 1940). Abdominothoracic injuries in the present series of abdominal injuries from this war approximate 13 per cent; the ratio is therefore not dissimilar to those of previous campaigns.

Statistics of abdominothoracic wounds culled from the official history of the war of 1914–1918 demonstrate that in a vast majority the abdominal lesion determines the gravity of the prognosis, and, further, that wounding of the

hollow abdominal viscera greatly augments the fatality of the injury. It will at once be apparent that the anxieties occasioned by a wound of the left dome of the diaphragm must greatly exceed those which are aroused by right-sided penetration of the midriff. An analysis of cases from this war confirms the truth of both these statements.

Of 78 abdominothoracic injuries in this present series, 42 were right-sided and 36 were left-sided. Forty-nine patients survived, i.e., a recovery rate of 63 per cent, a figure which very nearly equals that attained by 6 surgeons of the Fourth Army in 1918 during the last great war. In this present series, 70 per cent of the patients with right-sided abdominothoracic wounds lived; whereas only 50 per cent of the left-sided abdominothoracic patients survived.

An excellent classification of penetrating abdominothoracic wounds has been given by my friend Tudor Edwards:

1. The chest and abdomen may be penetrated by separate missiles, the wounded man sometimes becoming a veritable St. Sebastian, his abdomen and chest riddled with fragments of high explosive or machine gun bullets.

2. Missiles may penetrate the chest, and may emerge through the abdominal wall or be retained within the belly; on the other hand, the track of the missile may be in the reverse direction—the wound of entry in the abdomen and the fragment retained within the thorax.

3. Traversing wounds of the lower chest, especially if inflicted during expiration, may pass through the diaphragm and occasion damage to the abdominal organs lying immediately subjacent to the midriff.

4. Tangential wounds of the lower thorax in which considerable damage, including diaphragmatic injury and perforation, is produced by the missile and in-driven fractured ribs.

The diaphragmatic lesion. The present war series confirms many of the findings of a quarter of a century ago. The injuries of the diaphragm in abdominothoracic lesions are still mostly found in the sloping muscular portion, and are especially frequent when this lies in contact with the thoracic wall. In cases that come to operation the rent is usually small; in one series the linear tear was half an inch long or less in 50 per cent of the cases. Many openings are mere punctures; larger irregular apertures in those suitable for surgery are seldom found to be more than 1½ to 2 inches in diameter.

Lockwood and Nixon (1918) compared the cardiac and respiratory embarrassment due to a rent in the diaphragm to that produced by an open pneumothorax; on the other hand, for Sauerbruch the importance of the diaphragm in relation to respiration and the circulation was exaggerated. The great improvement in the recovery rate of abdominothoracic cases after the diaphragm began to be sutured by British surgeons in the last war may have been partly due to the repair of that muscle, but also to the improved treatment of the thoracic condition and increasing familiarity with the many problems of war surgery. Small wounds undoubtedly heal spontaneously, and others are at least temporarily plugged by omentum, spleen, liver, stomach, etc.

Wounds of the central tendinous part are obviously more serious than those at the periphery, but some have survived. A century ago Guthrie published notes of a man with a wound of pericardium, left ventricle lung, liver, and the tendon of the diaphragm. The man survived for 4 or 5 months; he suffered from palpitation and uneasy sensations in the chest, and died of bronchitis. Fuchsig (Sauerbruch and O'Shaughnessy, 1937) successfully operated upon a patient with a stab wound of the right ventricle which also perforated the central portion of the diaphragm. The track passed obliquely inwards from the fifth sternochondral articulation and was thought before operation to implicate the stomach.

Diagnosis of penetrating abdominothoracic wounds. Doubt may sometimes be felt at first whether the gravity of the condition of a man with an abdominothoracic wound is due to the thoracic, to the abdominal, or to other concomitant injury. Nixon (1919), who had great experience of these cases, thought that if there is a fair air entry into the lungs thoracic injury is not to be held accountable.

The anatomical site of the aperture of entry and of exit in a traversing wound of the trunk limns the track of the missile with fair accuracy. The position of the patient at the time of

injury also demands consideration; the structures probably damaged may then be readily adumbrated. In cases in which a fragment of metal, spicules of broken rib, etc., are retained, radiological investigation is indispensable; its necessity in estimating diaphragmatic movements and thoracic pathology cannot be overestimated. There are also clinical signs and symptoms which arrest attention and which may clarify, or may, on the other hand, obscure, the diagnosis:

1. Abdominal rigidity does not of necessity betoken involvement of the subphrenic viscera. It is well known that injuries of the pleura or lung, especially if situated in proximity to the diaphragm, may occasion abdominal rigidity and may arouse suspicion of an abdominal lesion.

2. Sickness and vomiting have been known to occur in cases of lower thoracic injury, but are more frequent in abdominal lesions, as is eructation of gas.

Diaphragmatic injury is suggested by an almost entirely thoracic type of respiration, with a catch at the end of inspiration, sometimes a definite spasm or hiccup; yet the actual respiratory rate may be little altered. In the late stages of injury to the diaphragm there is fixed pain, exaggerated on exertion and referred to clavicle or scapula according to the position of the injury or location of the retained missile. Pain is induced especially by lifting, coughing, or even deep respiration. The diaphragm is kept motionless on the affected side.

The diagnosis of a wound of the diaphragm is not easy in subparietal injuries. The syndrome of tension pneumothorax may be simulated by the sudden irruption of stomach or colon into the chest. Radiology and the determination of the intrapleural pressure enable a correct diagnosis to be attained.

The existence of *blast contusion of the lung* is now well established on clinical and x-ray evidence and by postmortem findings, and the dangers attending the use of inhalation anesthesia in these cases are overwhelming; great caution must therefore be employed when this is suspected; yet blast contusion of the lung is sometimes only the index of perhaps graver changes in the organs below the diaphragm. Other serious cases may have been in very close proximity to detonating bombs, and may be suffering from a dangerous and grave degree of saturation of the blood by explosive gases, such as carbon monoxide or nitric oxide. The severity of the clinical state may even be due to such lesions as myocardial trauma. Such possibilities should not be overlooked amid the circumstances of this "total" war; their presence and the existence of other grave multiple injuries heavily load the scales against recovery.

Penetrating injuries by large missiles. The injuries produced inside the chest or abdomen by large fragments of metal or other foreign body are almost always irrecoverable; the result is scarcely likely to be different in those wounds if more than one cavity of the body is implicated. There was in the Royal College of Surgeons' Museum till the time of its destruction a piece of brass tubing, 4⅜ inches long, removed by Mr. Reginald Vick in Macedonia from a Greek soldier, who recovered after the simple extraction of the missile, which had passed from the middle of the right scapula and projected in the epigastrium (Gordon-Taylor, 1939).

Saint (quoted by Gordon-Taylor) had a successful right-sided abdominothoracic case in which a fragment of shell weighing 2 ounces had traversed chest, diaphragm, and liver and produced 2 perforations of the duodenum and 1 in the hepatic flexure of the colon.

In one of my patients, the successful result of whose case is recorded elsewhere, a missile weighing nearly 4 ounces produced the most grievous damage inside the belly and fractured the bony wall of the thorax (Gordon-Taylor, 1919); the diaphragm was apparently uninjured. In the penetrating abdominothoracic wounds which form a section of the series collected from this war, there is no record of any case that controverts the reputed fatality of the large missile when it wounds the trunk.

Treatment of penetrating abdominothoracic injuries. This contribution is largely concerned with the surgical treatment of injuries of the diaphragm and of those abdominal organs whose anatomical proximity renders them specially vulnerable in cases of diaphragmatic wounding.

Treatment of wounds implicating the liver. The dimensions and the velocity of the missile play an important part in determining the type of hepatic lesion, which may be almost protean in character; large fragments of liver may be torn off, and as much as one-third of the right lobe has been found loose in the peritoneal cavity of a patient who recovered from a right-sided penetrating abdominothoracic injury in the last war.

Before their total destruction, the specimens in the Royal College of Surgeons' War collection illustrating gunshot wounds of the liver revealed many lesions for which any surgery must be futile or incomplete; thus it would be impossible by operative measures alone to prevent infection throughout the length of a ragged track running from the right lateral surface of the organ to its extreme pole on the other side of the body. In many cases of liver injury due to enemy action there are few arresting clinical signs, and it is significant that out of all the penetrating injuries of the abdomen which recovered in the last war without operation the wounds were mostly situated in the liver area. Surgical intervention directed towards the liver is indicated under the following circumstances only: (1) gross hemorrhage from the liver, which mainly depends on whether large veins in the organ have been injured—hemorrhage otherwise ceases spontaneously, as does oozing of bile, unless main ducts are severed; (2) the association of some thoracic or another abdominal lesion demanding exploration; (3) the retention of a missile in the liver, especially a large missile in an accessible position in that organ. In the case of severe laceration of the liver packing may be necessary to control hemorrhage. In some such patients the diaphragm may be sutured, and the thorax closed in the approved manner with airtight drainage of the pleura by means of a Malecot's tube inserted through a separate intercostal incision. The gauze pack is brought out through another separate incision in the anterior abdominal wall. In other cases the diaphragmatic opening may be enlarged parallel with fibers from mediastinal to lateral border; the diaphragmatic edges are now approximated to the intercostal muscles and the pleura is thus shut off from the drainage track.

Early jaundice in cases of hepatic injury may be present, and is usually slight and evanescent; the possibility of a collection of bile in peritoneum or pelvis should always be considered. Late jaundice has a much graver significance, and indicates serious infection.

Secondary hepatic hemorrhage in penetrating abdominothoracic injuries is almost always fatal, and is usually associated with signs of sepsis such as pain, elevation of temperature and pulse rate, abdominal pallor, restlessness, and loss of strength.

The formation of an intrahepatic abscess round a retained fragment may be dealt with successfully by surgical measures.

Treatment of gunshot injury of the spleen. A study of the specimens of gunshot injury of the spleen in the war collection formerly housed in the Royal College of Surgeons used to suggest that wounds of that organ are frequently complicated by damage to adjacent viscera; yet in some collected clinical series it is stated that in more than half the cases of splenic injury revealed at operation there was no damage to other abdominal organs. This was certainly not my experience (Gordon-Taylor, 1939), which is in agreement with that of Major Jolly in his surgical work with the Spanish Republican Army (Jolly, 1940).

The propriety of primary splenectomy in cases of gunshot injury still remains a subject of controversy. The removal of the organ should certainly not be resorted to lightheartedly, but in my opinion the procedure has not greatly increased the risk. The suture of the spleen may not be difficult when the organ is approached through the chest and diaphragm, but when explored by other routes cobbling of the organ is wasteful of time and may leave a sense of insecurity. Jolly (1940) and some of the Spanish surgeons write enthusiastically of splenectomy.

Numerous cases of successful transdiaphragmatic splenectomy in left-sided abdominothoracic wounds were recorded in the war of 1914–1918, some of which were associated with the operative repair of injuries to the stomach (Richard Charles, George Gask, J. E. H. Roberts, A. L. Lockwood, Gordon Bryan, Gordon-Taylor, etc., and very recently by Valentine Logue). In the last war recovery has even

taken place in cases of left-sided abdominothoracic wounds in which left-sided nephrectomy as well as splenectomy had to be performed for complete disruption of each organ (Gordon-Taylor) and also in the present conflict (J. Scholefield).

Treatment of wounds of the pancreas. These injuries were less frequent in the war of 1914–1918, or at any rate were less often recognized, than injuries of any other of the abdominal viscera; it is not otherwise today. The intimate anatomical relation of the gland to the large blood vessels doubtless explains the paucity of wounds coming under the observation of the casualty hospital surgeons; doubtless some are unrecognized and are designated retroperitoneal hematomas. I have knowledge of only 3 abdominothoracic injuries implicating the pancreas in which recovery took place in the last war (Saint, Alan Curry, Gordon-Bryan); there are none in the present series from this conflict.

Treatment of injury to the kidney. Each kidney is equally liable to damage. It was estimated that in 40 per cent of gunshot wounds of the kidney investigated at an English surgical base in France during 1914–1918 the thorax was also implicated. The propriety of immediate operation on the kidney in abdominothoracic wounds demands even more careful consideration than in purely abdominal injuries. Probably the best course is to excise the wound leading down to the damaged kidney; the organ can then be inspected and any foreign body removed.

In the majority of cases the renal injury plays a minor part in menacing life, and only for severe hemorrhage, a hopelessly pulped organ, or gross damage to the renal pedicle is primary nephrectomy indicated. In about 20 per cent of cases of gunshot injury of the kidney in the last war, life was threatened by secondary hemorrhage, consequent on sepsis, a retained missile, or an infarct of the kidney produced by damage to some branch of the renal artery; secondary hemorrhage is an infrequent phenomenon today.

Treatment of injury to the hollow organs. Of hollow organs the stomach and splenic flexure of the colon are those most liable to injury; in suitable cases transdiaphragmatic laparotomy affords excellent access to these organs. Concomitant involvement of the small intestine denotes a more vertical track of the missile, and demands a separate approach or a much extended incision; such a measure, though necessary, increases risk to life. Multivisceral damage also augments mortality, and vertical wounds, which may even extend from supraclavicular fossa to femur, tend to be very fatal.

The possibility of injury to the duodenum must always be borne in mind, and any hematoma in its vicinity should be suspect, lest a retroperitoneal rupture of this fixed part of the small gut be overlooked. Every abdominothoracic case in the present series associated with a laceration of the hepatic flexure has perished.

Summary of treatment. The treatment of penetrating abdominothoracic injuries may be summarized as follows:

1. In many traversing (through-and-through) abdominothoracic wounds of the right side produced by a small bomb fragment or bullet *no immediate active surgical treatment* is required, provided that: (a) no gross damage has been inflicted upon the thoracic or abdominal wall—fractured ribs, explosive effect, etc.; (b) the direction of the track of the missile does not appear to compromise the general peritoneal cavity or suggest the desirability of its exploration; (c) the signs of abdominal hemorrhage or of injury to a hollow viscus are clearly absent.

2. In cases of right-sided abdominothoracic wounds in which a small fragment is retained in an inaccessible position in the substance of the liver an *expectant line of treatment* is the correct procedure; accessible fragments, unless small, should be sought and removed.

3. When there is an open, blowing thoracic wound or an associated "stove-in chest," the chest injury must of course assume chronological priority of treatment.

4. If the position of the wound of entry and exit in a left-sided abdominothoracic wound adumbrates a track implicating that fatal left subphrenic area of the abdomen, or if a radiograph demonstrates a fragment of metal retained in this region, the thorax should be dealt with first and access to the upper abdomen obtained through the diaphragm.

Fig. 1. Entrance Hall of the Royal College of Surgeons of England showing the destruction effected by the bombing on the night of May 10–11, 1941.

Fig. 2. Room 3 in the Museum of the Royal College of Surgeons showing the destruction of the room and its galleries. The bust of John Hunter is enclosed in a rampart of bricks.

Fig. 3. Room 5 which contained the majority of the comparative anatomy specimens belonging to the Museum which started with the original Hunterian collection.

Fig. 4. This shows amid the débris of Room 4 the bust of the naturalist, Owen, a former conservator, which was only partially damaged.

5. When the thoracic injury appears insignificant, but there is evidence of severe widespread intraperitoneal damage, especially involvement of hollow viscera, the abdomen should be explored through an appropriately placed laparotomy incision. This instruction applies to wounds of thorax and abdomen produced by the same or by separate missiles.

6. When the thoracic injury seems slight, and when the evidence of a radiograph or the direction of a missile track in a through-and-through wound suggests an extraperitoneal course of a small fragment, such an abdominothoracic injury may often be left alone.

If in such cases there is evidence of injury to the kidney, the parietal wound down to the kidney should be excised, the organ investigated, and any foreign body removed.

7. In cases in which the thoracic wound is situated low down on the lateral or anterolateral aspect of the chest, access to both supradiaphragmatic and infradiaphragmatic areas may be obtained by cutting through the costal arch after the manner of Bland-Sutton, Duval, Bérard, etc.; this method of access is indubitably severe.

8. If an abdominothoracic injury has been approached from the abdominal aspect, it is important not to waste time trying to complete a difficult suture of the diaphragm in a critically ill patient, *unless* the aperture in the midriff is so large that immediate or early herniation of the abdominal contents is certain to occur.

Nonpenetrating abdominothoracic injuries. There are no successful operations for subparietal abdominothoracic injuries indisputably involving the diaphragm in this present series of cases. The inference is that these cases involve such desperate or multiple injuries that death ensues; some such cases are found at autopsy. The experience of this war so far goes to show that abdominothoracic injuries due to fragments of high explosive or bullets are far less grave than those due to crushing force or the effect of blast.

A man of 50 years was admitted to hospital after having been dug out from under the débris of a house. He showed no marks of external injury, complained of no pain, distress, and was only slightly shocked. On the following morning he was dyspneic and complained of pain in the left chest, these symptoms increasing during the day. On examination he was tympanitic over the left chest up to the third rib anteriorly, and his heart was displaced to the right. An x-ray suggested a diagnosis of collapse of the left lung, a pneumothorax and a pleural effusion. Just above the fluid level were some vague shadows which were thought possibly to indicate the presence in the thorax of gut. However, on the supposition that the condition was a tension pneumothorax, a needle was inserted in fourth intercostal space anteriorly and about a liter of air was let out with great relief to the patient. The process was repeated, and the needle was connected with a receiver by means of rubber drainage. Fluids taken by the mouth escaped through the needle in the thorax(!) The patient was finally operated upon, and a tear in the diaphragm found, through which an enormous hernia of the stomach had taken place. Death occurred.

Mention has already been made of the advancement of the science and craft of surgery through the stimulus of war. The familiarity with the transdiaphragmatic approach to the vault of the abdominal cavity attained in the latter years of the war of 1914–1918 has been turned to useful purpose by thoracic surgeons since the war. The advances in this field are stupendous. Diaphragmatic hernia, especially that produced by injury is nowadays approached by the thoracic route in Britain; the operation of cardio-omentopexy gave good results in the late Mr. O'Shaughnessy's capable hands, and improvements in the technique of the operation have been effected by Mr. John B. Hunter. The general surgeon also avails himself of a thoracic approach in the operation for the surgical removal of the lower end of the esophagus or of the cardiac end of the stomach.

Increasing familiarity with thoracic surgery doubtless provided the stimulus for Pierre Duval's successful operation for the extraction of a bullet from the suprahepatic portion of the inferior vena cava; the sternum was split, and the diaphragm divided backwards to the caval opening in the midriff. To my mind, this still remains the most brilliant operation in the history of surgery.

CONCLUSIONS

1. Despite the gravity of the wounds and the frequent association of multiple injuries, approximately 50 per cent of the patients with

abdominal injury for whom operation is possible survive.

2. The military situation permits of no information as to the percentage of all abdominal casualties for which operation is possible.

3. The percentage of recoveries for injuries to the stomach, the small intestine, and the spleen is actually higher than in 1914–1918, though the recovery rate for the large bowel is the same.

4. Few patients have survived after lengthy resections of bowel.

5. The employment of the sulfonamide locally and by oral administration has proved of inestimable value.

6. The transfusion of blood or the blood derivatives has been employed on a liberal scale and this method of treatment has made a host of patients operable who would otherwise certainly have died.

THE CARE OF THE LIGHTLY WOUNDED

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THE main thesis of my remarks is that far too little attention was paid in the last war to the care of the lightly wounded. By lightly wounded I mean wounds which do not involve any of the body cavities, such as the head, chest, or abdomen, or any bone, major blood vessel, or nerve. Most of these patients were ambulatory and, had they received prompt surgical attention, should have been able to return to duty within a few weeks. As a group, they represented a considerable majority of all the wounded.

We were told that the main duty of the Medical Corps was to maintain the strength of the fighting forces, yet the primary attention, as well as the large majority of the time and effort of the surgeons, was directed to the care of the severely wounded, very few of whom ever went back to duty. The lightly wounded "waited for the second table and got the leavings." This was quite in keeping with our peace time training and humanitarian desires. If our main object is to save life, those dangerously wounded should come first; but if our main object is to win the war and maintain the fighting forces it would seem that the men who might go back to duty should receive at least equal attention and that the attempt should be made to reduce their period of disability to the minimum.

As I am expressing a purely personal and individual opinion I may be allowed to recount the experiences on which that opinion is based, limited though they were. Going over with the Presbyterian Hospital Unit in May, 1917, we were assigned to the British Expeditionary Force, and No. 1 General Hospital at Etretat near Havre was turned over to our care. At the time of our arrival in France things had been relatively quiet for some time and most of the patients then in the hospital had been sent down from the front area several weeks before. The main problem seemed to be to get the severely wounded patients well enough to be sent across the channel to England. These included patients with badly infected compound fractures, chest wounds, and a few who survived after abdominal injury. Also there was a large number of ambulatory patients with small infected wounds, many of whom had been under treatment for weeks and even months. In addition to their local wounds they had become soft and flabby, and their morale very low. When their wounds finally healed, they were sent to convalescent camps for more weeks of rehabilitation before going back to the rest areas to rejoin their divisions. When a train load of 300 to 700 new patients arrived at the base, all hands concentrated on the severely wounded and those patients with minor injuries waited until all the others had been cared for. As the wounds by that time were 3 to 10 days old, not much was done except daily dressings by the junior medical officers, or more usually, the nurses.

After the Somme, the British Expeditionary Force realized that the wounded could be handled better if their operative treatment was carried out nearer the front lines. In preparation for the battle of Passchendaele in July, 1917, operating teams were sent from the base hospitals to the casualty clearing stations which were stationed 5 to 10 miles behind the lines and usually at a railhead. The patients came from the field hospitals to the casualty clearing station by ambulance and from there were sent down by train. They usually reached the hospitals 4 to 12 hours after injury. These hospitals were entirely housed in tents except for a Nissen hut for the operating theater. When we arrived on July 23, 1917, there were 3 groups of these hospitals back of Ypres with 3 or 4 hospitals in each group. We were assigned to No. 47 Casualty Clearing Station with 7 other surgical teams. Each team consisted of a surgeon, an anesthetist, a nurse, and an orderly. The duties of the

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operating team were twofold, to serve in the admitting ward and in the operating theater. In the former, wounds were merely inspected, dressings changed, and the decision made as to whether the patient should go to the resuscitation ward, preoperative ward, or be held for evacuation on the next train. When a rush was on, the admitting and sorting was done by one of the other medical officers. The operating teams were on duty 16 hours out of the 24 so there were 6 teams operating from 8 a.m. to midnight, and 4 from midnight to 8 a.m. The plan in our group was for the ambulances to bring all patients to one hospital until 200 had been admitted, the stream then being diverted to the second hospital. By the time the third had admitted its quota, the first hospital was supposed to have finished with its group and be ready for the next. During a push, of course, the numbers were far greater than in the intervening times. During a lull it might take 24 hours to get our quota of 200 but on the second day of the first push we rotated 6 times, each hospital getting over 1200 patients. The worst cases, except for those patients obviously moribund, were operated on first. One severe case an hour was about the average that one team could handle. This meant that during the busiest period only 10 per cent of the patients received could be handled in the operating theater. The rest had to be sent on to get their operative care later on, perhaps the next day, perhaps a week later. This failure to give the lightly wounded early operative treatment was a necessity during rush times but the peak load necessity seemed to establish the general policy at all times, and general policies in the British Expeditionary Force or any army are hard to change. This I discovered during one quiet period when only 2 teams were on call. I took my team to the receiving tent and under gas operated on some of the patients with minor wounds who, as I had seen at the base hospital, required months to get back to duty. If operated upon early I thought they might recover within a few weeks. We were able to care for quite a few cases in a short time. Soon word came from the Commanding Officer "Sorry, but that's not done in the B.E.F." This same general plan seemed to hold in other casualty clearing stations in our area. The French had already established the wisdom of early surgical treatment of minor wounds and during quiet times were doing a good deal of it in their advance hospitals. Coming back to the base hospital, I was again impressed with the long delay in healing of those minor wounds whose only early treatment was dressings, or occasionally some bipp paste.

After 14 months with the British I was transferred to the American Expeditionary Forces in the latter days of the battle of Château-Thierry. During this and the St. Mihiel drive the problem was to meet the actual necessities with the materials at hand, but later in the Argonne, with more hospitals and better organization, the problem of providing the wounded with early surgical treatment was well met. In addition to a goodly number of evacuation hospitals, well equipped and with surgeons of experience, several mobile hospitals, notably Nos. 1, 2, and 4, were set up sufficiently far forward to give the severely wounded an excellent chance for recovery. Yet here again, in both evacuation and mobile hospitals the major emphasis was placed on giving the severely wounded the right of way. The others were either attended to after the severe cases were finished, or were immediately sent down the line. In a few places operating teams were assigned to the lightly wounded group. Sherbondy and George Davis by using 3 tables, orderlies, and nurses proved that they could handle 6 to 8 cases an hour. At the time of the Armistice, Colonel Grissinger of the First Corps had plans all ready for execution for a special hospital well forward for the lightly wounded patients only, but it was never opened.

That early operative treatment of minor wounds will shorten tremendously the period of disability was proved at the hospital for the Army of Occupation in Coblenz. In the first month we had 83 cases of gunshot wounds all due to careless handling of firearms. This led one old regular to say "I always claimed that a soldier was the last person in the world to be trusted with firearms."

I have a vivid memory of a dressing station along the road that ran north from Ypres

along the canal. Here in a small cellar an attempt was being made to revive a patient with a badly shattered thigh and a perforating belly, while huddled up behind what was left of the front wall of the house was a group of walking wounded waiting for transportation. Again at the field ambulance tired men were working over a row of stretchers, while near by a large group of walkers squatted down or curled up on the ground waiting for transportation. Near by was the narrow gauge railroad with its cars of shells coming up, and the cars going back—empty. Lorries were going up the road full of supplies of one sort or another and others going back—empty; yet the walking wounded waited for ambulances. Again at the casualty clearing station when the ambulances arrived—patients on stretchers were cared for first while the walkers waited. Their dressings were changed, they were fed and herded to one side to await transportation by the next train to go down. I can see them when the train arrived at the base. Again the stretchers came first in the ambulances, while the walkers, who could, slowly plodded the half mile from the railway station to the hospital. It sometimes took 24 to 48 hours of operative work to care for the severely wounded before the others could have their turn. It was too late then for any preventive work and for early healing. One found just dirty, granulating wounds, often with insufficient drainage. Then came the long, slow weeks of healing with a gradual softening—physical, mental, and spiritual. This was "the forgotten man."

In the Argonne the picture was similar. In the divisional triage as the stream of wounded men came in they were sorted out and passed down to the mobile and evacuation hospitals. Again the major attention and time were given to the severely wounded while the lightly wounded received either delayed treatment or were sent directly on with a mere change of dressing. These were the men, however, who, if they could have had operative treatment early, might have rejoined their units within a few weeks. Of the patients with severe injuries of the head, chest, belly or with compound fractures and tight calves, very, very few ever resumed active duty.

So much for the past. Can we profit by that experience in planning for the days that lie ahead? In times of retreat and especially the conditions the British faced in the days preceding Dunkirk little can be planned or carried out. The main problem is to get the wounded away at all. Any operative treatment must be delayed until they have been brought a long way to the rear. In stationary warfare or in times of an advance, hospital facilities can be brought reasonably close, and operative treatment carried out early.

The surgical care of the lightly wounded varies from that of the more serious cases in several ways. Many of the latter patients need attention before they come to the operating table, hence the need for resuscitation wards for combatting shock. Such a measure is unnecessary for the lightly wounded. In the operating room there are three periods: first, the preparation of the patient and the induction of anesthesia; second, the operation itself; and third, the application of dressings and splints when necessary. In cases of major wounds the operation will require 60 to 90 per cent of the total time. One operator can use 2 tables at the most, the next patient being prepared as he operates and the last stage of operation being carried out by an assistant as the operator starts anew. With the minor wounds the time of operating may not be greater than that required for preparation and may be even less. One surgeon could handle 3 or possibly 4 tables with the appropriate number of assistants. While 1 serious case an hour can be used as a general figure for what one surgeon could handle, with proper assistants he could operate on 6 to 8 minor cases.

After operation the serious cases will need a good deal of careful attention for hours and even days. The organization of postoperative wards and personnel is quite different from that needed for the later care of the minor wounds. Many of the patients with serious injuries are actually nontransportable for days and will do much better if they are not moved for a much longer period. Most of the patients with minor injuries could be transported within a few hours or a few days at most. Therefore, is it not worth considering to arrange for entirely separate units to handle these 2

groups of cases? Each unit should be planned and organized according to the needs of the group assigned to it. As the stream of wounded starts back the two groups should be separated early. A large majority of the lightly wounded might be transported back in the supply trucks on their return journeys, the ambulances being used for the serious cases. Certain hospitals should be designated and planned only for the care of patients with minor injuries. Such hospitals should plan for a routine somewhat as follows. On arrival the patients would be examined by an experienced surgeon to pick out those sent by mistake who belong in the more serious group, and mechanism provided for their immediate transfer. The suitable cases then would go to the x-ray department for localization of foreign bodies. After this they would go to the preoperative ward for removal of clothing and rest until the operating theater was ready for them. In the operating room each surgeon would have 3 tables at his disposal and 3 teams. The patient would be placed on the first table, the first team preparing the field and giving the anesthetic. The same team would repeat this performance on the second and third tables. The surgeon and his assistant would follow after and débride the wound, treating by primary suture or packing with or without the use of chemotherapy and dictating orders for later care. The third team would then take over, apply the dressing, bandages, and any necessary splint. The patient would then be taken to the postoperative ward. If the lighter forms of anesthesia were to be used, either inhalation or intravenous, immediate aftercare of these patients would be much simpler than that of the more serious cases and would require a smaller personnel in these wards. With the exception of some of the lower extremity cases most of these patients would become ambulatory in a short period of time. This would simplify the feeding problem. At the time of operation the surgeon should be able to make a fair guess as to whether the patient should be retained or early returned to his unit or sent farther back for prolonged treatment. Final decision, of course, would have to be checked before discharge. This plan seems reasonable to me. In this way this "forgotten man" might be remembered and his minor wound prove to be a minor affair and not a cause of months of disability.

Many of us believe that the only kind of war casualties we will have to face in the near future, outside of the Navy, will be those resulting from bombs. Looking after the wounded civilian population may not be maintaining the fighting forces in the field and it may not be the duty of the Army Medical Corps, but it will have to be done. As plans are made to meet this emergency let us hope that such plans will include prompt attention to this group of lightly wounded. I was delighted to hear from a member of our staff who is now working in London that separate units have been established for this very purpose.

CONCLUSION

I feel strongly that the care of the lightly wounded as I saw it in France was greatly neglected. I sincerely hope that this will not occur when we have to meet the problem again. God grant that we do not have to, but should it come let us be ready for it.

PENETRATING WOUNDS OF THE HEART AND PERICARDIUM

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WOUNDS of the heart were recognized in Homeric times, but none was successfully sutured until 1896. The history of the intervening 2500 or so years of speculation, experiment, and trial has been related by Ricketts, Cutler and Beck, and by Elkin (10) and need not be repeated here. Since the first successful operation by Rehn in 1896, the recognition and treatment of this condition has become more frequent, until today hardly a month goes by without the report of successful suture of a cardiac wound. Review of the many single case reports in the literature probably gives an optimistic view of the mortality, since unsuccessful single cases are seldom reported. The results of a questionnaire, sent out by Bigger (5), to the members of the American Association for Thoracic Surgery, the American Surgical Association, and the Southern Surgical Association showed a mortality of approximately 50 per cent in 141 patients. Bigger (6) and Elkin (10), have reported series of 25 and 38 cases with mortality of 36 and 42 per cent in those cases which presented an opportunity for diagnosis and treatment. Prior to 1933, 3 wounds of the heart were recognized and operated upon at the Louisville City Hospital by Sherrill in 1913, Hill (7) in 1926 and Cox in 1927, the last case having successful termination. Since 1933, from 2 to 8 cases have been seen yearly. This large number probably indicates not so much an increase in the number of heart wounds as it does an increased awareness of and interest in, the condition, since the diagnosis depends primarily upon keeping in mind the possibility of cardiac injury in every case of wound of the thorax. Elkin states that at Emory University 2 per cent of the penetrating wounds of the chest injured the heart. In Bigger's experience, 0.1 per cent of admissions to his surgical service in Richmond are wounds of the heart. These figures closely approximate our findings at the Louisville City Hospital.

From the University of Louisville School of Medicine and the Louisville City Hospital.

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PATHOLOGY

Wounds of the heart may, of course, be caused by any sharp instrument or projectile. The weapon and the type of wound vary according to the local customs of the civilian population, or current military practice. In our experience, the knife, pistol, and ice pick have been the most frequent weapons. A weapon or projectile may reach the heart from an entrance anywhere on the chest or even the upper abdomen. In most cases, however, the wound of entrance is between the second and seventh left costal cartilages anteriorly, usually traversing the left pleura. Occasionally the heart is reached from a wound of the posterior thorax. The right ventricle is the most frequently injured on account of its anterior position. Next in order of frequency are the left ventricle, the auricles, and the intrapericardial portions of the great vessels. Sucking wounds of the pleura are not uncommon. Injury to the peripheral portion of the lungs is frequent but usually of little moment.

Wounds of the heart may or may not penetrate the cavities. Bleeding from coronary vessels and the heart muscle, while not so profuse as when the chambers are opened, is surprisingly brisk and may be rapidly fatal. The consequences of cardiac hemorrhage are due, in the main, to tamponade and exsanguination. The alternative between tamponade and exsanguination depends upon the relative flow capacities of the cardiac wound and the opening in the pericardium. Blood escaping from the heart fills the pericardium

and increases the intrapericardial pressure if denied free egress. Compression of the great veins at the base of the heart backs up the venous inflow and compensatory increase in venous pressure results. The blood pressure falls and the systolic and diastolic pressures tend to approximate each other because the heart is handling less blood. When the increasing venous pressure cannot overcome the intrapericardial pressure, circulatory arrest occurs. As little as 200 cubic centimeters of blood may cause fatal tamponade quickly if it escapes rapidly into the pericardium. On the other hand, a slow leak, as from an ice pick wound, may produce fatal tamponade several days later, as in Case A9. If the opening in the pericardium is of such size and location as to permit free and unimpeded flow to the exterior or into the pleura, tamponade does not occur but fatal hemorrhage ensues unless it is checked. As might be expected, many patients with large cardiac wounds and massive hemorrhage succumb before surgical aid is available. Death may occur in the hospital during the few minutes that it takes to make the diagnosis and start operation, even with the best organization.

Often the two conditions, tamponade and hemorrhage, occur simultaneously when the hole in the pericardium allows large quantities of blood to escape but not fast enough to decompress the rapidly filling pericardium. Occasionally, tamponade and extrapericardial bleeding occur alternately. In 2 cases in our series, increasing tamponade was evident until the intrapericardial pressure apparently reached the point where it could force open the communicating wound into the pleura. Spontaneous drainage into the pleura relieved the symptoms of tamponade, which recurred however, within a few minutes. Several such cycles were observed and, in 1 patient, could be brought about by changing position, which probably opened the wound in the pericardium. In a small proportion of cases, bleeding from the heart is small in amount and ceases spontaneously. If the pericardial opening in such cases allows decompression, recovery will ensue without surgical treatment.

Cerebral damage may occur as a result of emboli thrown off from mural thrombi in the cardiac chambers, or as a result of cerebral anoxemia produced by neglected tamponade. The intracranial pressure closely parallels the high venous pressure and, in Case A1 of our series, reached 400 millimeters of spinal fluid. This high intracranial pressure and coexisting low blood pressure reduce the flow of blood through the brain so that harmful and even fatal cerebral anoxemia may occur. Extrapericardial hematomas may produce enough compression of the heart to give rise to tamponade. Such hematomas most frequently arise from division of the internal mammary artery, as in Cases C1, C4, and C7.

DIAGNOSIS

The diagnosis depends primarily upon an alert house staff keeping in mind the possibility of cardiac injury in every case of wound of the chest, no matter how trivial. This is especially true when the evidence of shock is out of proportion to the apparent severity of the wound or loss of blood. Acute alcoholism often clouds the picture and, in our series, was present in all but 2 cases. When acute tamponade is present, Beck's triad of acute cardiac compression is found. This triad consists of (a) falling arterial pressure, (b) rising venous pressure, and (c) small, quiet heart (4). The patient appears to be in shock. The blood pressure, and particularly the pulse pressure, are low or unobtainable. The pulse is weak but not so rapid as might be expected unless there is considerable hemorrhage. Heart sounds are weak and distant. Increased venous pressure is evidenced by distended neck veins and cyanosis is often present. Direct measurement of the venous pressure at the elbow, by use of a water spinal manometer filled with 2½ per cent sodium citrate or normal saline solution, shows an increase often to 250 millimeters or more. Delirium, stupor, unconsciousness, or hemiplegia may occur, due to alcoholism, cerebral anoxemia, or emboli. Fluoroscopy is of the greatest value in diagnosis and clearly shows diminished or absent pulsation of the heart shadow. If available, a roentgen kymogram is of great aid.

When massive cardiac hemorrhage into the pleura is occurring, the exact diagnosis of

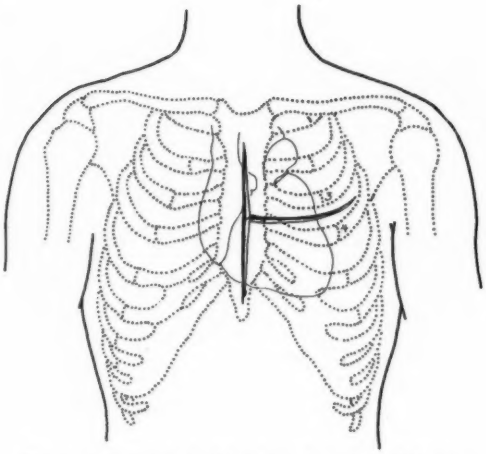


Fig. 1. A transverse incision is made over the interspace where the wound of entrance is located and the wound of entrance is excised with the incision. The vertical portion upward, downward or both is added later if necessary. Incision is always made on the left, except when the wound of entrance is far to the right.

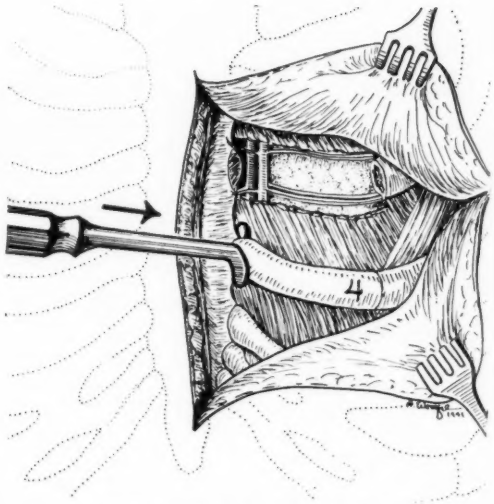


Fig. 2. After clearing of soft parts from the costal cartilage, a Doyen raspatory is introduced about the cartilage, close to the sternum, and pushed smartly in a lateral direction. This strips the soft tissues from the rib and enables one to do a rapid resection without injuring the pleura or the internal mammary artery since, if correctly inserted, the instrument invariably enters the proper plane of cleavage superficial to the pleura.

wound of the heart may be more difficult, but the indications for immediate operative intervention are clear and imperative. Bleeding from the parenchyma of the lung in wounds of the thorax may be massive but is slow and seldom requires operative hemostasis. On the other hand, free bleeding from the heart, great vessels, internal mammary, or intercostal arteries is fast and profuse. Rapidly progressive shock is present early and death may quickly ensue unless hemorrhage is checked. We believe, therefore, that in the presence of increasing hemothorax and rapidly progressive fall in blood pressure, particularly with a precordial wound, exploration should be carried out at once, for even though the heart be intact, the arrest of hemorrhage from other structures is imperative.

TREATMENT

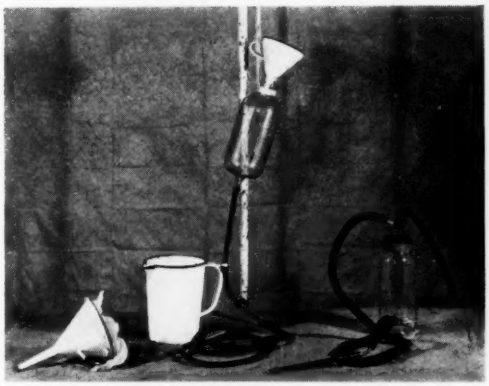
Once the diagnosis and the decision to intervene are made, operation should be immediate and no preoperative treatment for shock or other condition should be allowed to delay operation. Intravenous fluids, particularly blood, should be administered when hemorrhage has occurred but are of little value preoperatively in case of tamponade. Morphine is used sparingly, particularly in the presence of alcoholism and tamponade, because of its effect upon an already depressed respiratory center. Aspiration of the pericardium as recommended by Bigger may be a lifesaving measure to tide the patient over while preparations are made for operation. Speed, but not haste, in preparing for operation is essential. Every large general hospital should have available at all times a sterile setup of instruments and linens, and the operating room, with at least one nurse and orderly in attendance, should be open 24 hours a day. No short cuts should be taken, however, in the scrub up of the team or the preparation of the field of operation. Undue haste here may be followed by empyema and pericarditis later. We have had no deaths from infection, and believe that this is the result of the same careful preparation as is used for any elective procedure.

A minimum of inhalation anesthesia is advisable, although oxygen under positive pressure is usually necessary on account of

the open pleura. The soporific effects of shock, tamponade, or alcoholism are generally present, but deeper anesthesia is often necessary after the release of tamponade. Our preference is for intercostal novocain block, usually of the third to sixth nerves, supplemented by oxygen and the minimum of nitrous oxide.

The incision should be one which permits rapid and adequate exposure of the heart and is made to the left of the sternum unless the wound of entrance is far to the right. This is best accomplished by a generous transverse incision over the interspace in which the wound is located. The wound of entrance is excised with this incision. The transverse incision may be joined, when necessary, by a vertical incision over the sternum (Fig. 1). The costal cartilages above and below the incision are exposed and resected with about 1 inch of rib, by the method described by Meyer: "Previously, subperiosteal resection of the ribs with a pleura often as thin as a spider's web, was a task, especially in a moribund patient, extremely trying. The operation must be carried out with meticulous care and yet with great rapidity.... However, one can resect the ribs in a few seconds and the steps of the operation are simple and the pleura is not opened or injured. . . . The sternum must be exposed more than usual.... The raspatory is introduced quite close to the sternum at the cartilaginous portion of the rib. . . . This takes only a few seconds. Fat lies beneath, loose, and can readily be pushed aside. Here the Doyen raspatory is brought into play.

"It is inserted medial to the internal mammary artery and when pushed further in a lateral direction we resect the ribs extrapleurally as far as necessary and without danger to the pleura, because in this layer, the pleura is surprisingly easy to remove" (Fig. 2). The internal mammary vessels are ligated and divided and the triangularis muscle and endothoracic fascia opened. The pleura is reflected from the pericardium by blunt dissection, beginning at the lower angle of the wound. Often this may be done by inserting the finger between the pericardium and pleura in the triangle of safety where the pericardium is uncovered by pleura. The



e d f a b c

Fig. 3. Autotransfusion outfit used in all cases of hemorrhage into body cavities: *a*, Pool suction tip; *b*, 500 cubic centimeter bottle with two-hole stopper containing citrate solution; *c*, tube running to operating room suction; *d*, 1000 cubic centimeter graduate; *e*, funnel with gauze filter; *f*, intravenous outfit with Murphy drip.

finger is then swept cephalad, easily separating the two structures. As much as necessary of the sternum is rongeured away. If additional exposure seems advisable on account of an oblique wound, the vertical limb is added to the incision upward, downward, or both, turning back triangular flaps which allow the removal of additional cartilages. If tamponade is present, the blood-filled pericardium will be tense, blue, and quiet. If the opening in the pericardium is large, it may usually be exposed and is best enlarged with the least damage to the heart, by gently but firmly spreading it with the fingers. If no opening is seen, the pericardium is nicked carefully after lifting it with forceps or stay sutures and this opening spread as above.

Clots are quickly scooped out of the pericardium with the fingers and liquid blood removed by suction into the autotransfusion outfit (Fig. 3). With release of the tamponade the force and rate of the heart beat increase and bleeding becomes profuse, so that continuous suction is used from now on until the heart has been sutured.

Unless the wound is immediately visible and easily accessible, it is best to ignore the bleeding and insert a fine silk traction suture into the apex as advocated by Beck (2). There is nothing more disconcerting than to hold in

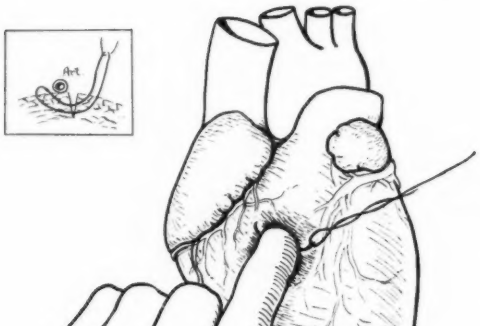


Fig. 4. Traction suture at apex, steadying heart while fine silk suture is being passed under finger which has been placed over the wound. Insert shows method of inserting mattress suture to avoid coronary vessel when wound is close to vessel.

one's hand a writhing, jumping heart and blindly attempt to find a wound deep in a gushing whirlpool of blood. The insertion of a traction suture converts this stage of the operation from futile blundering into an orderly process. The traction suture steadies the jumping organ so that a finger may be placed over the opening temporarily to staunch the flow. A word of warning to those inexperienced in cardiac surgery is necessary at this point. If held rigidly, the traction suture cuts through the myocardium with each systolic contraction. The hand holding the suture must therefore relax elastically with each beat, steadying but not fixing the heart. The finger must be placed over but not into the wound. One's natural tendency to insert the finger as a cork will only result in further laceration of the myocardium.

With the finger over the wound as temporary patch, a fine silk suture threaded on a French eye needle is inserted across the wound beneath the finger (Fig. 4). Slight traction on this suture holds the wound closed after the finger is removed and allows other necessary sutures to be inserted. None of these sutures must be so deep as to penetrate the endocardium, on account of the increased risk of mural thrombi. They should be tied only tight enough to give hemostasis and must avoid strangulation of the muscle. Injured coronary vessels may be covered with a small patch of pectoral muscle (3) if the vessel is not completely severed. Complete division of large coronary arteries requires ligation by suture. Never attempt to grasp a bleeding coronary vessel with a hemostat. The closure of wounds close to large coronary vessels may present a problem. In Case A14, death resulted from occlusion of a large coronary vessel by the suture. This may be avoided easily by an "on-end" mattress suture beneath the vessel, as shown in Figure 4 insert.

If the wound is on the right or posterior portion of the ventricles, it may usually be exposed by appropriate traction on the suture at the apex. If necessary, additional traction sutures well up on the ventricle may be used to rotate the heart to bring posterior wounds into view (Fig. 5).

Hemorrhage from wounds of the auricles and great vessels may be controlled temporarily by a soft clamp, such as the Trendelenberg artery clip or the Horsley arteriovenous fistula clamp, or even with ordinary hemostats prior to the placing of sutures.

The blood collected in the autotransfusion bottles should, by now, be running into the patient's veins. Any remaining blood in the pericardium and pleura is thoroughly sucked out for refusion. Autotransfusion in amounts up to 2500 cubic centimeters has been used in 14 of our cases. With the use of the apparatus illustrated, it is a simple, rapid procedure which is often life saving.

If there is already a free opening between the pericardium and pleura, this is left open and enlarged, if necessary, to allow adequate postoperative decompression of the pericardium into the pleura (11). This permits drainage of any remaining blood, as well as the increased pericardial fluid, which occurs after any operation upon the heart. Drainage to the exterior presents a real danger of infection, as the draining fluid is sucked in and out of the drainage tract with each respiration.

The anterior pericardium is closed loosely with interrupted fine silk sutures. Tight closure is unnecessary and may be impossible or even harmful because of the cardiac dilatation which frequently occurs in these cases (1, 10). Soft tissues of the thoracic wall are closed firmly in layers with interrupted fine silk and the wound sealed with silver foil, after reinflation of the left lung by carefully applied positive pressure.

Recently, we have implanted up to 5 grams of powdered sulfanilamide or sulfathiazol into the pericardium and pleura before closure, as these wounds are all potentially infected.

Operation may sometimes be avoided in patients who have only mild tamponade and who do not have progressive intrapleural hemorrhage. These patients should, however, remain in the hospital and be confined strictly to bed until all danger of recurrent tamponade has passed. Frequently repeated observations of blood pressure, pulse, and venous pressure should be made, as well as daily fluoroscopic examination, since late tamponade may occur as in Cases A3, A9, A27. If tamponade is serious enough to require aspiration, as advocated by Bigger, open operation with wound suture and drainage of the pericardium into pleura is the treatment of choice.

POSTOPERATIVE TREATMENT

The patient is placed in an oxygen tent immediately after operation and is left there until his respiratory rate returns to normal. Fowler's position is usually the most comfortable and assists respiration. If shock has not been relieved by operation and autotransfusion, additional blood or plasma are indicated. Sufficient morphine should be administered to allay pain and restlessness, but not to depress respiration. Any remaining air and blood in the pleural cavity should be removed by thoracentesis to keep the lung expanded. This may be repeated at intervals as fluid reaccumulates, due to the irritating effect of blood on the serosa of the pericardium and pleura. The use of heparin, as suggested by Bigger, may be advisable, particularly when the weapon has pierced the endocardium. This may prevent deaths from embolism, such as occurred in Case A21.

Fig. 5. Showing use of additional traction suture for rotating heart in either direction. Several such sutures may be used.

PROGNOSIS

The prognosis of wounds of the heart depends largely upon the character of the wound and the rapidity with which treatment is initiated. Undoubtedly, some patients die immediately because of disruption of the conducting mechanism of the heart. Many with large wounds succumb rapidly from hemorrhage before they can be transported to the hospital. This is particularly true of gunshot injuries with wounds of entrance and exit, often involving more than one chamber of the heart, as well as important extrapericardial structures. However, at least half the cases of massive hemorrhage and almost all the cases of tamponade, survive for an hour which, except in rural districts, should be time for transportation, diagnosis, and treatment. All patients, who died in the Louisville City Hospital before or during operation, were cases of hemorrhage, except 2 deaths from tamponade and 1 death on the table following occlusion of a major coronary artery. In those patients who survived operation, the most frequent fatal complication has been cerebral damage. This may be due to em-

bolism as in Case A21, or neglected tamponade and resultant cerebral anoxemia, as in Cases A1, A4, A12, and A18. In those patients who lived the symptoms and signs of cerebral injury have disappeared spontaneously within a few months without leaving residual damage. No cases of fatal infection have been observed. It is our opinion that infection is most often caused by undue excitement and haste in preparation, or by drainage of the pericardium externally. Clinical cardiac disability has been uniformly absent after operation and there has been no indication of reduced cardiac reserve. Electrocardiograph changes are usual following wounds of the heart, and vary from minor irregularities of the T-wave to the typical picture of major coronary occlusion, as shown in Case A24. These abnormalities improve and sometimes even disappear within a few months. A detailed analysis of these changes is to be reported at a later time.

CASES

During the last 8 years, 47 patients with presumed or proved wounds of the heart have been admitted to the Louisville City Hospital. Fourteen of these have been reported previously in detail, (1, 12, 13). Operations were performed by the senior author and, under his guidance, by the following resident surgeons at the Louisville City Hospital: J. M. Mayer, E. M. Drissen, H. G. Saam, V. A. Badertscher, C. M. Bernhard, C. M. Schroeder, C. H. Maguire, and E. S. Strode. In 7 cases, the presumption that the heart was wounded was not borne out, but interesting cardiac aspects justify their inclusion in this report. Death occurred in 13 cases within 20 minutes of admission before operation could be started. In no case was operation delayed or refused, because of the moribund condition of the patient. Five of the patients operated upon were on the table within 20 minutes of admission, having been brought directly from the accident room. In the 27 cases which presented an opportunity for diagnosis and treatment, there were 7 deaths, a mortality of 25.9 per cent (Table I). Five were treated conservatively, with 1 death. This patient refused to stay in the hospital and died of tamponade on the eleventh day. Twenty-two patients were operated upon, with 6 deaths. Two of these deaths were due to hemorrhage, 1 on the table and 1 30 minutes after operation. One died on the table following ligation of a major coronary artery and there were 3 deaths 18 hours, 48 hours, and 5 days after operation, due to cerebral complications. Our mortality has decreased with experience, so that in the last 13 cases there has been but 1 death.

Case A1. W. M., A28283, colored male, aged 40 years, with an ice pick wound in the left anterior axillary line in the sixth interspace, was seen in marked shock. No blood pressure was discernible, heart sounds were distant, pulse weak and 60 per minute. The patient had a lacerated scalp and other ice pick wounds and was observed for 18 hours and then prepared for subtemporal decompression because of hemiplegia and unconsciousness that had developed. Spinal fluid pressure was 400 millimeters. Fluoroscopy showed wide round heart shadow. The pericardium was explored and ice pick wound of left ventricle with tamponade found. The patient never regained consciousness and died 18 hours after operation, with cerebral manifestations and a terminal fever of 108 (13).

Case A2. J. D., A29433, colored male, aged 22 years, was sent directly from the emergency room to the operating room. There was a knife wound in the left anterior axillary line in the third interspace. The patient was in marked shock; no blood pressure was obtainable. Exploration revealed a 1 by 1½-inch laceration in the left ventricle and 3500 cubic centimeters of blood in the left pleural cavity. He died on the operating table from exsanguination (13).

Case A3. W. J., A31773, colored male, aged 35 years, was seen with a stab wound in the seventh interspace 2 centimeters to the left of the sternum. Blood pressure was 98/70. Roentgenogram showed slight enlargement of heart shadow. On the second day the patient collapsed on getting out of bed and went into extreme shock; he recovered slowly. The same thing was repeated on the fourth day. He was discharged on the twelfth day and readmitted 6 days later with edema of scrotum and legs, distant heart sounds and enlarged shadow. Uneventful recovery took place (12).

Case A4. V. H., 34195, colored male, aged 38 years, with a stab wound in the left anterior axillary line at the level of the sixth rib was admitted in marked shock. He improved under observation. X-ray picture showed wide heart shadow. Patient was observed for 22 hours and then exploratory operation carried out because of development of paradoxical pulse and right-sided twitchings. Laceration of posterolateral wall of left ventricle was found and sutured. Recovery took place. Patient was discharged on the thirty-fifth day (13).

CASE A5. W. C., 34388, white male, aged 11 years, with .22 caliber rifle wound in fourth interspace 3 centimeters to the right of the sternum was seen in marked shock. No blood pressure was obtainable; pulse was 70, heart sounds distant. Fluoroscopy revealed slight enlargement of the heart shadow. A laceration in the upper lateral portion of the right ventricle was closed. Patient was discharged on the thirty-fifth day (13).

CASE A6. J. S., 38543, colored male, aged 35 years, was stabbed in the right chest with scissors. Sucking wound was present in the fourth interspace. Blood pressure varied greatly on observation. Venous pressure was 150 millimeters of water. X-ray film of chest revealed hemopneumopericardium with a definite fluid level. His hospital course was uneventful and patient was discharged on seventeenth day (13).

CASE A7. C. T., 43640, colored male, aged 26 years, with gunshot wound in the fifth interspace in the left anterior axillary line was seen in marked shock. No blood pressure was obtainable; heart sounds were distant; pulse 80 per minute. Wound in the lower portion of the left ventricle was found and sutured. No wound of exit was found. Recovery was uneventful. Patient was discharged on the forty-second day. X-ray film showed bullet in right iliac artery. Distal pulsation was absent but circulation adequate (12).

CASE A8. T. R., 44460, colored male, aged 17 years, with laceration of chest, beginning in left fifth interspace in midclavicular line and extending across sternum to 2 centimeters on right was in moderate shock. Blood pressure was 74/50; pulse, 100 per minute. Patient was operated upon within 45 minutes after admission. Laceration of right auricle was found and sutured, but patient had lost too much blood and died 30 minutes after operation (12).

CASE A9. A. C., 44937, white female, aged 29 years, was stabbed repeatedly with an ice pick. There was subcutaneous emphysema throughout most of the chest wall. Fluoroscopy showed enlarged cardiac shadow with decrease in pulsation. Patient refused to stay in hospital and died 11 days after injury while straining at stool. Autopsy revealed a puncture wound of the left auricle that had apparently oozed slowly and caused fatal tamponade (12).

CASE A10. E. H., 43909, colored male, aged 48 years, with 4 stab wounds in the third interspace on the left was in marked shock. Blood pressure was 46/40; heart sounds, distant; pulse, paradoxical and 80 per minute. Fluoroscopy showed enlarged heart shadow. Three lacerations in the left ventricle were sutured, and recovery was uneventful. Patient was discharged on the thirty-fourth day (12).

CASE A11. F. W., A52994, colored female, aged 28 years, was seen with stab wound in the sixth interspace just to left of sternum. Neck and arm veins were distended. Patient was in moderate shock; blood pressure was 80/60; heart sounds, muffled; pulse paradoxial and 100 per minute. Laceration of right ventricle sutured. Recovery was uneventful. Patient was discharged on the twenty-sixth day.

CASE A12. L. R., 1623, white male, aged 27 years, was seen with 6 centimeter laceration in the fourth interspace in the precordium. Heart sounds were distant; blood pressure, 40/0; pulse, 80 per minute. Neck veins were distended. Internal mammary and right auricle were lacerated. They were sutured successfully but patient remained unconscious and died at end of 48 hours with a terminal fever of 108 degrees, due either to cerebral anoxemia or postoperative heat stroke. Autopsy showed the heart wounds to be sutured satisfactorily.

CASE A13. E. C., 2322, colored male, aged 23 years, with stab wound in right fourth interspace 4 centimeters from sternum was seen in marked shock. Blood pressure was unobtainable; heart sounds, quite distant; pulse, weak and recorded as 40 per minute. Laceration of right ventricle on the upper anterior aspect found and sutured. Recovery was uneventful. It is interesting, in this case, that there was moderate bleeding to the outside and when operation was carried out, it was found that there was obliteration of both pleural cavities. Patient was discharged on the twenty-sixth day.

CASE A14. M. L., 26018, colored female, aged 20 years, with stab wound in fourth interspace 2 centimeters to left of sternum was seen in marked shock. Blood pressure was unobtainable; heart sounds, distant; pulse, weak, 60 per minute. Laceration of right ventricle was adjacent to the descending coronary artery. Coronary vessels were tied during suture of the wound. Typical acute cardiac dilatation and death on the table followed (1).

CASE A15. C. B., 26804, colored male, aged 34 years, with transverse laceration that involved the seventh and eighth costal cartilages and nicked the sternum was seen in marked shock. Blood pressure was unobtainable; no radial pulse palpable; heart sounds quite distant, 100 per minute. Laceration of the midportion of the right ventricle was sutured. Recovery was uneventful. Patient was discharged on the eighteenth day.

CASE A16. B. A., 3088, colored male, aged 34 years, with stab wound in the sixth interspace just to the left of the sternum was seen in moderate shock. Blood pressure was 94/64; pulse, 96 per minute; neck veins, distended; venous pressure, 250 millimeters of water; heart sounds, muffled. Fluoroscopy revealed enlarged nonpulsatile shadow. Laceration of tip of the anterior surface of the right ventricle was sutured. Recovery was uneventful. Patient was discharged on the eighteenth day.

CASE A17. E. G., 29910, white female, aged 36 years, had received three ice pick wounds in the third interspace just to right of sternum, also a wound in the posterior chest just to the left of the vertebrae. Blood pressure was 70/50; pulse, 120 per minute; neck veins, distended; venous pressure, 200 millimeters of water; heart sounds, distant; patient

in mild shock. Fluoroscopy revealed enlarged nonpulsatile shadow. Wound in anterior portion of the aorta just above the valves was closed with 1 silk suture. Recovery was uneventful. Patient was discharged on the fifteenth day.

CASE A18. L. S., 31825, colored male, aged 30 years, walked into the emergency room and collapsed. He was in marked shock. Patient had received stab wound in the fourth interspace 4 centimeters to left of the sternum. Blood pressure was 78/60; pulse, 120 per minute. There was slight venous distention; venous pressure, 190 millimeters of water; heart sounds of fair quality. Fluoroscopy showed large nonpulsatile shadow and kymogram, limitation of ventricular excursion. There was laceration in the left ventricle with a hematoma over the anterior descending branch of the left coronary vessels. Infection of skin flaps developed and then osteomyelitis of the ends of the fourth and fifth ribs. There also developed a left facial weakness. Patient was discharged in 57 days with both these conditions cleared up.

CASE A19. S. W., 5186, colored male, aged 42 years, had received stab wound just to the left of the ensiform cartilage. Patient was in marked shock; blood pressure, 44/0; muffled, irregular cardiac sounds; pulse, 60 per minute, paradoxical in type. Neck veins were distended, and venous pressure 260 and 280 millimeters of water on successive readings. Fluoroscopy showed enlarged nonpulsatile shadow. Laceration of right ventricle on the anterior inferior aspect was sutured. Recovery was uneventful. Patient was discharged on the fifteenth day.

CASE A20. A. B. L., 77941, colored male, aged 17 years, with stab wound in the fifth interspace just beneath the left pectoral fold was seen in profound shock. Blood pressure was 40/20; neck veins were distended; venous pressure was 280 millimeters of water; heart sounds, distant; pulse, 60 per minute. Fluoroscopy revealed large nonpulsatile shadow. Laceration of the left ventricle 3 centimeters in length was sutured. Recovery was uneventful. Patient was discharged on the fifteenth day.

CASE A21. J. W. B., 80020, colored male, aged 23 years, had received stab wound in the fifth interspace in left anterior axillary line. Blood pressure was 60/40; pulse, 100 per minute. Neck veins were distended; venous pressure was 190 millimeters of water; heart sounds distant with paradoxical pulse. Fluoroscopy showed enlarged nonpulsatile shadow. Laceration of lateral side of left ventricle was sutured. Patient died on the fifth day with complete right-sided hemiplegia. Autopsy showed large mural thrombus at the site of wound in endocardium and an embolus plugged left middle cerebral artery.

CASE A22. L. J., 80755, colored male, aged 36 years, had received ice pick wound in the third interspace 5 centimeters to the left of the sternum and 2 other wounds slightly above and lateral to this one. Patient was in shock. Blood pressure was 60/50; pulse, 84 per minute. Heart sounds were distant; there was slight venous distention; venous pressure was 110 millimeters of water; fluoroscopy showed enlarged nonpulsatile shadow. Exploration revealed tamponade and 2 wounds of the arch of the aorta. Recovery was uneventful. Patient was discharged on the thirteenth day.

CASE A23. L. H., 80854, colored male, aged 39 years, with gunshot wound of left chest in the fourth interspace was seen in marked shock. Pressure was 40/0; pulse, 70 per minute; neck veins, slightly distended; venous pressure, 180 millimeters of water; no audible heart sounds. Fluoroscopy revealed a wide nonpulsatile shadow and the bullet in the right lung. Exploration disclosed a fractured sternum and tamponade. The bullet had driven a fragment of sternum into the wall of the right ventricle. Recovery was uneventful. Patient was discharged on the fourteenth day.

CASE A24. J. D. H., 51196, colored male, aged 19 years with stab wound in the fourth interspace 4 centimeters to left of sternum was seen in marked shock. Blood pressure was unobtainable; pulse, 80 per minute. Patient was taken direct to operating room without fluoroscopy or venous pressure readings. A laceration of the left atrioventricular groove 4 centimeters in length which had severed the anterior descending branch of the left coronary was sutured. Recovery was uneventful. Patient was discharged on the thirty-eighth day. Electrocardiogram showed typical anterior coronary block. This has improved to the present date.

CASE A25. J. C., 81194, colored male, aged 22 years, was admitted 7 hours after having been stabbed in the sixth interspace just posterior to anterior axillary line. Patient complained of occasional precordial pain, slight dyspnea, moderate venous distention. Venous pressure was 150 to 160 millimeters of water. Fluoroscopy showed wide cardiac shadow and kymogram showed decreased ventricular excursion. Patient was comfortable with exception of slight dyspnea. He was discharged on the ninth day.

CASE A26. W. H., 52765, white male, aged 25 years, with stab wound in 1 centimeter medial and below left nipple was seen in moderate shock. Blood pressure was 80/40; pulse, weak and rapid; heart sounds faint. Venous pressure was 160 millimeters of water. Fluoroscopy showed decreased pulsation. No hemothorax was present. Laceration of left ventricle 1.5 centimeters in length was sutured. Recovery was uneventful.

CASE A27. J. T., 84218, colored male, aged 25 years, was seen with 2 stab wounds in left third interspace 4 centimeters from midsternal line and just below xyphoid at left costal margin. There was no shock. Blood pressure was 130/80; pulse, 130. Venous pressure was 110 millimeters of water; sounds were normal except for succussion splash. X-ray film showed hemopneumopericardium. No operation was done. On the second day blood pressure was 86/60 and venous pressure 250 millimeters of water. Spontaneous improvement occurred, however, and uneventful recovery ensued.

TABLE I

Case	Year	Sex	Age	Weapon	Time from wound to operation	Location	Result	Remarks
A 1	1933	M	40	Icepick	18 hrs.	L V	Died	18 hours after operation cerebral damage
A 2	1933	M	22	Knife	30 min.	L V	Died	On table from hemorrhage
A 3	1933	M	35	Knife	No operation		Lived	Hemopericardium, mild tamponade
A 4	1934	M	38	Knife	23 hrs.	L V	Lived	Hemiplegia, full recovery
A 5	1934	M	11	Rifle	70 + min.	R V	Lived	Stitch abscess, full recovery
A 6	1934	M	35	Scissors	No operation		Lived	Hemopneumopericardium
A 7	1935	M	26	Pistol	80 + min.	L V	Lived	No exit. Bullet in iliac artery
A 8	1935	M	17	Knife	90 min.	R A	Died	On table from hemorrhage
A 9	1935	F	29	Icepick	No operation	L A	Died	Refused treatment. Died in 11 days
A10	1935	M	48	Knife	2¼ hrs.	R V	Lived	Three wounds of heart
A11	1936	F	28	Knife	2½ hrs.	R V	Lived	
A12	1937	M	27	Knife	20 + min.	R A	Died	48 hours after operation cerebral damage
A13	1937	M	23	Knife	20 + min.	R V	Lived	
A14	1938	F	20	Knife	15+min.	R V	Died	On table. Coronary ligation
A15	1938	M	34	Knife	3 hrs.	R V	Lived	
A16	1938	M	34	Knife	80 + min.	R V	Lived	
A17	1938	F	36	Icepick	75 min.	Aorta	Lived	
A18	1939	M	30	Knife	2 hrs.	R V	Lived	Osteomyelitis of ribs. Facial palsy. Full recovery
A19	1939	M	42	Knife	90 + min.	R V	Lived	
A20	1940	M	17	Knife	70 + min.	L V	Lived	Coronary branch divided
A21	1940	M	23	Knife	100 min.	L V	Died	5 days after operation cerebral embolus
A22	1941	M	36	Icepick	2 hrs.	Aorta	Lived	
A23	1941	M	39	Pistol	80 min.	R V	Lived	Heart lacerated by fragment of sternum
A24	1941	M	19	Knife	20 + min.	LVandA	Lived	Anterior coronary occlusion
A25	1941	M	22	Knife	No operation		Lived	Hemopericardium. Mild tamponade
A26	1941	M	25	Knife	45 min.	L V	Lived	
A27	1941	M	25	Knife	No operation		Lived	Hemopneumopericardium

Of the 13 patients who died before operation could be started, 7 were due to gunshot wounds. All succumbed within 20 minutes of admission and autopsies showed that all died of rapid massive hemorrhage, except 2 in which death was due to tamponade (Table II).

CASE B1. J. L. W., 46313, colored male, with stab wound medial to the left nipple, was in profound shock on admission, and died within 20 minutes. Autopsy revealed a stab wound in the third interspace 9 centimeters to left of sternum. There was 3000 cubic centimeters of blood in the pleural cavity on the left. Right ventricle had a laceration 3 centimeters in length near interventricular septum. The anterior descending branch of the right coronary had also been severed.

CASE B2. J. R., 44018, colored male, aged 43 years, with gunshot wound in the fourth interspace 10 centimeters to left of sternum, lived about 10 minutes after reaching the emergency room. Autopsy revealed a gunshot wound of both walls of the right ventricle, a perforation of the aorta, 500 cubic centimeters of blood in the pericardial sac, and both pleural cavities full of blood.

CASE B3. F. D., A50401, white male, aged 35 years, had received 2 stab wounds, one anteriorly in the third interspace just to left of sternum and the other in posterior axillary line at the level of the sixth rib. Patient was in marked shock and expired within 10 minutes. Autopsy revealed laceration of left ventricle near the interventricular septum, 200 cubic centimeters of blood in pericardial sac and 2500 cubic centimeters of blood in pleural cavities.

CASE B4. T. J., A60534, colored male, aged 24 years, died on arrival on the ward. There was a gunshot wound of left arm and the left chest in the sixth interspace in left anterior axillary line. Autopsy revealed the bullet to be in the right chest wall under

TABLE II

Case	Year	Sex	Age	Weapon	Time from admission to death	Location	Remarks
B 1	1935	M	?	Knife	20 min.	R V	3000 c.c. hemothorax
B 2	1935	M	43	Pistol	10 min.	R V and aorta	Hemothorax
B 3	1936	M	35	Knife	10 min.	L V	Hemothorax
B 4	1937	M	24	Pistol	On arrival	R and L V	Hemothorax
B 5	1937	M	30	Knife	On arrival	L V	Tamponade and hemothorax
B 6	1937	M	24	Knife	On arrival	L V	Hemothorax
B 7	1937	M	35	Pistol	On arrival	R and L V	Hemothorax
B 8	1937	M	24	Knife	On arrival	Aorta	Hemothorax
B 9	1939	M	22	Knife	5 min.	L V	Tamponade
B10	1940	M	45	Pistol	10 min.	R V	Hemothorax
B11	1941	M	44	Pistol	On arrival	Aorta	Hemothorax
B12	1941	M	30	Pistol	On arrival	Pulmonary artery and L V	Hemothorax
B13	1941	M	24	Pistol	10 min.	R and L V	Hemothorax

the fifth rib, 7 centimeters to right of sternum. There was 2000 cubic centimeters of blood in pleural cavities; pericardium was full and there was a wound through both ventricles.

CASE B5. S. W., B89301, colored male, aged 30 years, with stab wound in the first interspace 2 centimeters to left of sternum, died on admission to emergency room. Autopsy revealed acute tamponade. Pericardial sac contained 200 cubic centimeters of blood. There were 1000 cubic centimeters of blood in each pleural cavity. A laceration of the left ventricle near the atrioventricular groove was found.

CASE B6. T. J., B90011, colored male, aged 24 years, with stab wound of the sixth interspace 14 centimeters to left of sternum, died on admission to emergency room. Each pleural cavity contained 1000 cubic centimeters of blood and pericardium was full. There was a laceration of wall of the left ventricle which extended into the interventricular septum.

CASE B7. C. S., B90063, colored male, aged 35 years, with gunshot wound at the sixth rib 2 centimeters to left of sternum, was dead on arrival. There was 400 cubic centimeters of blood in pericardium and approximately 1000 cubic centimeters in each pleural cavity. There was a through-and-through wound of the heart involving both ventricles and the septum.

CASE B8. J. S., 11992, colored male, aged 24 years, with stab wound just below midportion of left clavicle, was dead on arrival. Both pleurae were full of blood, pericardium contained 100 cubic centimeters. There was a through-and-through laceration of the ascending aorta just above the valves.

CASE B9. D. McC., 78674, white male, aged 22 years, with stab wound of the fifth intercostal space, just to left of sternum, arrived in emergency room breathing but died by the time he reached the ward. Acute tamponade was present with 450 cubic centimeters of blood in pericardial sac and a 1.5 centimeter laceration in wall of right ventricle 2 centimeters from apex.

CASE B10. R. G., 82850, colored male, aged 45 years, had received gunshot wound of the sixth intercostal space 2 centimeters to left of sternum, with a wound of exit posteriorly 6 centimeters to left of midline at level of the twelfth rib. Patient expired in 10 minutes. There was a wound of the right ventricle which was 3 centimeters from the apex and 1000 cubic centimeters of blood was in each pleural cavity.

CASE B11. L. B., 83162, colored male, aged 44 years, with gunshot wound in anterior axillary line with no wound of exit, was dead on arrival. There was a laceration of the aorta 6 centimeters above the valves with 500 cubic centimeters of blood in pericardial sac, 1500 cubic centimeters of blood in left pleural cavity, and 1700 cubic centimeters in the right.

CASE B12. L. E., 83641, colored male, aged 30? years, with gunshot wound of the second interspace in left midclavicular line, expired on arrival. There was a wound along the wall of the left ventricle and of the posterior wall of the pulmonary aorta. There was 300 cubic centimeters of blood in pericardium and 1200 cubic centimeters of blood in each pleural cavity.

CASE B13. J. P., 37803, colored male, aged 24 years, had received gunshot wound at left sternal border in the fifth intercostal space. Heart sounds were distant. There was no palpable pulse; blood pressure was not discernible. Patient died in 10 minutes while being prepared for operation. Through-and-through wound of both ventricles was present with hemothorax of 3000 cubic centimeters.

TABLE III.

Case	Year	Sex	Age	Weapon	Result	Remarks
C1	1934	F	43	Knife	Lived	Venous pressure 250 extrapericardial hematoma
C2	1937	F	31	Pistol	Died	Wound of pericardium and diaphragm
C3	1937	M	25	Knife	Died	Internal mammary hemorrhage and hemothorax
C4	1937	M	29	Knife	Died	Internal mammary hemorrhage and extrapericardial hematoma
C5	1938	M	40	Knife	Lived	Acute cardiac dilatation
C6	1940	M	32	Pistol	Lived	Hemothorax
C7	1941	M	24	Pistol	Lived	Extrapericardial hematoma

Of the 7 cases in which the presumption of wound of the heart was not borne out at operation, 3 had tamponade due to the pressure of extrapericardial hematomas. In 2 there was massive intrapleural arterial hemorrhage and in 1 a wound of the pericardium and diaphragm but not of the heart. The most interesting of this group, Case C5, acute cardiac dilatation, relieved by pericardiotomy, has been discussed in detail by Badertscher (Table III).

CASE C1. H. T., 38700, colored female, aged 43 years, with stab wound in the fourth interspace 5 centimeters to left of sternum was seen in moderate shock. Blood pressure was 68/20; pulse, 82 per minute; venous pressure, 250 millimeters of water. There was present a laceration of pericardium and about 100 cubic centimeters of blood in pericardium but no definite cardiac wound. However, there was a large extrapericardial hematoma from the internal mammary artery with pressure on the pericardium, causing tamponade. Course was uneventful. Patient was discharged on the twenty-fourth day.

CASE C2. E. R., A57031, colored female, aged 31 years, had received pistol wound in the fifth interspace 1 centimeter to left of sternum, exit posteriorly in the seventh interspace. Patient was in marked shock. Blood pressure was unobtainable; heart sounds, distant; pulse, 100 per minute. Progress was progressively downward. Patient was taken to operating room after 2 hours, and exploration revealed an old adhesive pericarditis. The bullet had torn off some of the inferior part of the pericardium but there was no definite cardiac wound. The bullet had then perforated the diaphragm medial to the wound in the pericardium. Patient died 24 hours after operation, never coming out of shock.

CASE C3. C. B., A59647, white male, aged 25 years, with sucking stab wound in left sixth interspace, was not in shock, but was explored because of position of the wound. Exploration revealed the left internal mammary artery severed but no heart wound. Patient died on the seventh day, apparently from secondary hemorrhage.

CASE C4. E. R., A59647, colored male, aged 29 years, with stab wound in the third interspace 3 centimeters to right of sternum, was in marked shock. Blood pressure was 84/50; sounds were of good quality; there was slight venous distention. Exploration revealed the right internal mammary cut and 1000 cubic centimeters of blood in right chest. Patient died on the fourth day after operation.

CASE C5. W. O. S., 25733, colored male, aged 40 years, had received stab wound in the third interspace 2 centimeters to left of sternum. Blood pressure was 82/50; pulse, 70 per minute. Sounds were distant; slight venous distention was present; moderate shock. No pericardial wound was found but pericardium was quite tense and when it was cut the heart bulged into the opening and blood pressure came up to a normal level. Patient had an uneventful recovery and was discharged on the fifteenth day. (Discussed in detail by Badertscher.)

CASE C6. W. H., 81802, white male, aged 32? years, with gunshot wound of the fifth interspace 5 centimeters to left of sternum, was seen in marked shock. Blood pressure was 40/20; pulse, 100 per minute; slight venous distention present. Fluoroscopy revealed no definite cardiac pulsation and the left chest was full of blood. No cardiac wound found on exploration. Left chest contained 1000 to 1500 cubic centimeters of blood. Patient signed out of hospital on the sixth day, but prior to that time his course had been uneventful.

CASE C7. S. W., 14929, colored male, aged 24 years, with gunshot wound in the third interspace 5 centimeters to left of sternum, was seen in marked shock. Blood pressure unobtainable; slight venous distention present; pulse, 120 per minute. Fluoroscopy showed no definite cardiac pulsation. Operation disclosed no definite cardiac wound, but a hematoma from left internal mammary artery causing tamponade. Recovery was uneventful. Patient was discharged on the eleventh day.

SUMMARY

Reports of successfully treated wounds of the heart are becoming more frequent because of better diagnosis and more aggressive treatment. Death usually occurs from either massive hemorrhage or tamponade. Most of the patients who die before operation succumb

to hemorrhage, usually due to gunshot wounds, although in our experience several patients with massive hemorrhage from gunshot wounds have survived following very early operative treatment. Patients with tamponade are much more likely to live long enough for treatment to be instituted and in only 2 of our preoperative deaths was this caused by tamponade. Of the 27 patients in our series who were alive 20 minutes after admission to the accident room, there were 7 deaths. This is a mortality of 25.9 per cent in those cases which presented an opportunity for diagnosis and treatment. That the results improve with experience is shown by the fact that in the last 13 of these cases, there has been but 1 death. Cerebral damage, due either to embolism or to anoxemia from neglected tamponade, has been the most frequent postoperative complication. No residual cardiac disability has been observed in patients who recovered. Acute cardiac tamponade may be produced by extracardiac lesions, such as hematomas.

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NONPENETRATING TRAUMA OF THE ABDOMEN

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TRAUMA to the abdominal viscera without laceration or penetration of the abdominal wall or with incomplete penetration presents a particularly fascinating problem and challenge to the surgeon, because of: (1) the high mortality attending laceration or rupture of the viscera; (2) the comparative infrequency with which the individual surgeon encounters abdominal trauma; (3) the frequent difficulty in making an accurate diagnosis of a serious lesion because of the apparently inconsequential or obscure initial symptoms; (4) the possibility of a variable latent period before evidence of extensive visceral damage appears; (5) the need for the recognition of the pitfalls in diagnosis and treatment if the extraordinarily high mortality is to be lowered.

Injury to the abdomen may result in: (1) a simple laceration or puncture of the abdominal wall, which does not perforate into the peritoneum; (2) a penetrating or perforating wound; (3) a contusion or subcutaneous rupture only of the abdominal wall; (4) a contusion, laceration, or rupture of an intra-abdominal organ or structure with no evidence of external injury; (5) any combination of the above four lesions (Levering).

Nonpenetrating trauma of the abdomen will include, then, a contusion or subcutaneous rupture of the abdominal wall, or a contusion, laceration, or rupture of intra-abdominal viscera or blood vessels, either without external injury or with a superficial unrelated nonpenetrating laceration.

MORTALITY

Mortality in subcutaneous abdominal visceral trauma is high largely because of the frequency of multiple major injuries which are inevitably and rapidly fatal. However, the reported mortality rate in recent years has shown a definite decrease. This decrease seems due to improvement in methods of diagnosis and better recognition of the therapeutic indications, especially the appropriate time for surgical interference.

TABLE I.—MORTALITY

Author	Years	No. cases	Mortality per cent
Petersen	1885–1890		60–70
Petersen	1900		30
Demel	1933 to	126	21.9
Lewis and Trimble	1936	140	20
Just		79	13.9

INCIDENCE

The incidence of subcutaneous trauma of the abdomen as compared to injuries elsewhere in the body is low. In a 5 year period, 2217 injuries of all types were admitted to our clinic only 32 (1.4 per cent) of which had nonpenetrating abdominal trauma. Cody reports similarly 5744 accidental deaths in Iowa during a 3 year period, 53 (0.9 per cent) of which were the result of subcutaneous abdominal trauma. A higher rate of occurrence might be found in densely populated areas where the likelihood of this type of injury as a result of motor accidents would be greater. However, it is obvious that nonpenetrating abdominal trauma is not too frequently encountered except possibly in hospitals devoted largely to traumatic surgery.

ETIOLOGY

Abdominal trauma may result from: (1) an anteroposterior or a lateral squeezing, or a direct blow, crushing a viscus between the instrument of force and the spine or rupturing an organ or the diaphragm by a great increase of intra-abdominal pressure; (2) a tangential force, moving the bowel or other viscus beyond its limits of mobility causing tears in mesentery, etc.; (3) compression of fluid or gas in a single loop of intestine; (4) fragments of pelvic bones, rupturing or puncturing the bladder and rectum; (5) falls at play, at work, or at home. Motor and indus-

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trial accidents, athletic injuries, and falls in the home are the most frequent causes. Of Bailey's 100 cases, 76 were due to transportation accidents (60 motor), the 24 remaining to industrial or athletic accidents, or falls in the home.

PATHOLOGY

In mild cases, usually without evidence of superficial contusion, there may be a hematoma deep in the abdominal muscles, secondary to a laceration of a muscle or a blood vessel, a retroperitoneal hematoma, hemorrhage into the mesentery or omentum or beneath the capsule of liver, spleen, or kidney, or subserosal hemorrhage of stomach or intestine. It is this group that definitely may be treated conservatively. The frequency with which mild indeterminate trauma is found has been variously reported: in 45 (30 per cent) of 140 cases by Lewis and Trimble, 41 (54 per cent) of 76 cases by Just, and 36 (38 per cent) of 94 cases in our series.

Crushing and severe injuries produce particularly laceration or rupture of the liver, spleen, pancreas, kidney, small or large intestine, stomach, diaphragm, bladder, gall bladder, omentum, or mesentery often accompanied by fracture of the pelvis, spine, or ribs. Numerous reports of obscure and rarer lesions have also been recorded such as: (1) hemoperitoneum due to subcutaneous rupture of the iliac vein; (2) mesenteric thrombosis; (3) rupture of a gastric ulcer; (4) avulsion of the gall bladder; (5) pancreatic cyst; (6) tuberculous peritonitis, following rupture of an intraperitoneal tuberculous abscess.

DIAGNOSIS

The successful outcome of most cases hinges upon the sagacity and diagnostic acumen of the attending physician. Clinically, abdominal trauma may be classified into three groups: (1) severe multiple injuries which are rapidly fatal and for which no treatment is of avail; (2) cases that obviously require immediate operation; (3) cases in which the diagnosis is doubtful and the indications for or against operation are not clear.

In the proper care of this third group lies the greatest opportunity for saving lives and lowering the extraordinarily high mortality rate. Very close and repeated observation is mandatory. At the earliest possible interval following the accident, a decision must be reached whether or not the lesion demands immediate operation.

Aids toward an accurate diagnosis will be: (1) the history; (2) careful physical examination; (3) blood count, blood protein estimations, urine examinations; (4) radiography.

History. It seems generally agreed that force applied to a *limited* or circumscribed area of the abdomen is more prone to lacerate or rupture the intestine or kidney, but force applied diffusely over a wide area is likely to injure the liver, spleen, pancreas, bladder, or blood vessels. Engorgement or dilatation during physiological activity may predispose to injury. Hence it is important, to know the exact character of the blow, the size of the object inflicting the trauma, the details of the accident, the time that has elapsed since the accident, and the previous consumption of food or drink as well as the record of any previous abdominal disease. A detailed and accurate history will aid in estimating the likely extent of the injury.

Examination. The examination of the patient should be thorough and painstaking with consummate weighing of the evidence. The pulse and blood pressure should be noted; a patient with pallor should suggest hemorrhage or primary shock. One of the deceptive features of abdominal trauma is that the primary shock may be transient. Certain cases that are apparently in shock may have a definite elevation of blood pressure. This hypertension has been shown to be due to extensive retroperitoneal hemorrhage or injury particularly about the kidney or adrenal. Retroperitoneal involvement must be suspected, therefore, with hypertension in abdominal trauma. If the patient is in shock, a detailed examination must be postponed until treatment for its relief has been effective. However, the examination, when made, should be complete for injury not only of the abdomen, but of other parts of the body, as multiple injuries are not infrequent.

Abdominal distention or meteorism, localized pain and tenderness, muscle rigidity or spasm, absence or presence of peristalsis and

the type of respiratory excursion must be carefully studied. Early abdominal distention with general abdominal, but not boardlike, rigidity and absence of severe pain, particularly if there is evidence of a concomitant back injury, are indications of injury or irritation of the celiac plexus, and that a conservative policy can be planned. *Increasing* abdominal distention with localized tenderness and rigidity—often boardlike—severe, *persistent*, or recurrent pain, and absence of peristalsis, are indications of a visceral injury, and for immediate operation. Rectal or vaginal examination, particularly when the lesion is in the lower abdomen, may prove of great value. By this procedure, a retroperitoneal rupture of an air-containing viscus may be recognized when palpable emphysema of the pelvis is present.

Either continuous or intermittent pain that is *persistent* and *repeated* vomiting or hematemesis, rising pulse rate, and spreading local tenderness are particularly significant. Vomiting, in itself, is not pathognomonic, but repeated vomiting, or repeated hematemesis and persistent pain may be evidence of visceral injury.

One should not be deceived by a posttraumatic period of comparative comfort or relative normalcy. Years ago (1858), Polland noted in certain instances of grave abdominal trauma, "the absence of all symptoms *indicating a mortal injury* for upward of two hours." Butler observes that with shock or alcoholism this interval may be lengthened to 6 or 8 hours. Berry has ascribed the *lack* of early significant symptoms in intestinal rupture to the fact that the immediate effect of severe injury to the intestine is a contraction of the bowel in the neighborhood of the lesion which tends for a time to prevent further extravasation of intestinal contents. This contraction may last for many hours. Cases of laceration of the intestine, stomach, bladder, and spleen have been recorded in which the patient has walked and shown no evidence of major casualty only to collapse later.

Blood count and laboratory tests. Immediate, complete blood count and urine examination should be made. Bloody urine indicates kidney, bladder, or urethral injury. If hemorrhage is suspected, estimation of the blood specific gravity by the falling-drop method of Barbour and Hamilton can be rapidly made, the concentration of blood plasma protein quickly determined, and prompt information obtained concerning the extent of blood loss. The estimation of blood concentration, if desired, can be checked by hematocrit determination; indications for type and amount of intravenous therapy may thus be obtained.

Radiography. A procedure that is of distinct value in the diagnosis of *intestinal* laceration or rupture is a radiograph of the abdomen. White has suggested that this be taken in the sitting posture so that free gas in the peritoneum can be better recognized by its concentration beneath the diaphragm—a crescent or sickle-shaped gas accumulation over the liver and below the diaphragm. If the patient cannot sit, White advises a lateral x-ray at the level of the diaphragm with the patient prone. Gas beneath the diaphragm when present is positive evidence of intestinal rupture, but *if absent or unrecognized it does not rule out the possibility of intestinal laceration.* Also, gas demonstrable in the retroperitoneal tissues may accompany duodenal rupture.

Intravenous urography and, in carefully selected cases, retrograde cystography and pyelography will be a great aid in the accurate diagnosis of urinary tract lesions, particularly lacerations of bladder and kidney.

Burke and Madigan have suggested the use of thorotrast as an aid in the diagnosis of lacerations of the liver and the spleen. Thorotrast is administered intravenously and an abdominal film is taken 4 hours later.

Peritoneoscopy. Peritoneoscopy may eventually prove of value in the diagnosis of certain obscure lesions but this procedure has not yet been in use sufficiently long to speak with authority concerning its applicability or indications in cases of abdominal trauma. It would seem to be contraindicated where gastrointestinal rupture is suspected. Its field of usefulness is likely to be limited.

Summary. The evidence as elaborated by history, examination, laboratory tests, and x-ray, must be carefully weighed. Abdominal examination is the most important. Severe localized or general persistent abdominal pain,

increasing pulse rate, repeated vomiting, localized tenderness and boardlike rigidity, with or without evidence of increasing hemorrhage or infection, form a combination that demands operative interference.

All cases, no matter how trivial, in which a decision for operation cannot be immediately made, should be kept under the closest observation and opiates withheld. Repeated examinations should be made at least every 30 minutes until a definite conclusion concerning operation can be reached. In an obscure quiescent case, illuminating symptoms such as pain, distention, or rigidity may have a sudden onset. Blood pressure and pulse records should be taken every 15 or 30 minutes. Blood counts should be repeated at short intervals. The repeated blood count may show evidence of hemorrhage by decreasing hemoglobin and red blood count and of advancing infection by an increasing leucocytosis. Decision for or against operation should be made within 4 to 6 hours after the accident. Any delay beyond this period may jeopardize the possibility of saving a life.

As Just has stated, "In spite of the most painstaking study, there will always remain a number of cases in which a definite diagnosis is impossible, but the syndrome is of a type which *justifies operation*. In these cases, an exploratory laparotomy should be done."

SHOCK

Primary shock may be due to: (1) extremely painful trauma; (2) severe crushing injury; and (3) hemorrhage, (Butler). Shock is not a necessary accompaniment of every injury; moreover it shows wide variations that may not be at all correlated with the severity of the trauma. Shock should be combatted promptly by application of heat, lowering of the head, elevating of the feet, intravenous infusions of blood plasma, administration of oxygen, and injection of eschatin or adrenal cortical extract, neosynephrin, veritol, or ephedrine. If blood plasma is not available intravenous administration of gum acacia, saline and glucose, or whole blood transfusions should be used. Morphia should be withheld until a decision concerning operation has been reached. Immediate operation should not be undertaken until an effort to relieve shock and improve the patient's condition has been made, and a systolic blood pressure of 100 or over is obtained. However, patients in shock requiring immediate operation should be treated and observed in accident wards or in or close to operating suites so that as little delay as possible occurs in inaugurating operative procedure as soon as the patient's condition justifies it.

Jaki distinguishes three stages of progression in severe abdominal trauma: (1) shock; (2) transient subjective improvement; (3) collapse in the case of hemorrhage, or peritonitis in the case of perforation (injury) of a hollow organ.

TREATMENT

Successful treatment to obtain eventual recovery depends upon: (1) prompt recognition that intra-abdominal trauma is present; (2) prompt decision that an operation is necessary; (3) the correct time for and method of operative interference; (4) the magnitude of the injury. With multiple extensive injuries early or immediate fatality may be inevitable—the extent of the trauma placing the injured beyond the aid of any treatment.

Treatment may be either conservative or operative.

Conservative treatment is largely symptomatic but may require maintenance of fluid balance and adequate blood concentration by appropriate intravenous therapy and transfusions, especially when vomiting or hemorrhage recurs and particularly in preparation for surgical intervention, early or late. In rupture of the hollow viscera, either actual or suspected, particularly of the intestine or bladder, some form of sulfonamide therapy is definitely indicated—sodium sulfathiazole intravenously, or sulfanilamide by hypodermoclysis is preferable, as it is not likely that these drugs will be readily tolerated by oral administration. Lesions of the hollow viscera will demand early operation, but solid visceral injuries, unless accompanied by persistent and unrestricted hemorrhage, may more properly be considered candidates for temporary conservative measures and for delayed or late operation.

Operation may be indicated either early or late. Early operation should take place within 6 hours of the accident, particularly when injury to hollow viscera seems likely. Late operation will be demanded by evidence of progressive or recurrent hemorrhage, extensive visceral damage or local tumor formation indicating unresolved hematomas, local abscesses, or actual neoplasm (pancreatic cyst, etc.).

The common intra-abdominal lesions are lacerations or rupture of the liver, spleen, kidney, intestine, and bladder. Their specific treatment will be briefly outlined:

Liver. When the patient is not moribund and when there is definite evidence of unchecked hemorrhage, operation is indicated. Without evidence of severe and persistent hemorrhage conservative treatment should suffice though with late recurrent hemorrhage operation may be required. Transfusion or blood plasma may be necessary before, during, and after operation. On exploration, if there is still bleeding from the liver this may be arrested by digital compression of the hepatic artery and portal vein at the foramen of Winslow and the laceration may be sutured or the hemorrhage controlled by tamponade and suture. Drainage should be instituted to facilitate the extra-abdominal escape of bile leaking from the laceration. If, on exploration, the hemorrhage seems controlled or has ceased it has been suggested that blood in the peritoneal cavity may be gently evacuated by suction, but clots in the rent in the liver had best not be disturbed as fatal and uncontrollable hemorrhage has occurred from overzealous efforts to suture a laceration when hemorrhage has ceased. Suture in this case is not necessary as spontaneous healing can take place. Trimble has pointed out the danger of reinfusion or transfusion of the blood taken from the peritoneal cavity in rupture of the liver. Toxic symptoms may follow, several fatal results have been recorded. Mortality rate from liver rupture is approximately 50 per cent due largely to the inefficacy of any treatment in extensive laceration.

Spleen. If the patient's blood pressure is low or he is in shock—blood plasma or a transfusion should be administered. Operation should take place as soon as the blood pressure is over 100, and transfusion should be continued during and following the operative procedure. The intraperitoneal blood may be ladled or aspirated out into a sterile flask, citrated, and reinfused into a vein. This may often prove a life-saving measure. Spinal anesthesia has much to recommend it. Splenectomy is to be preferred to suture or tamponade of the laceration. The mortality rate is 30 per cent largely because of associated extensive trauma.

Kidney. Most of the injuries to the kidney are contusions, which heal spontaneously, and expectant treatment will suffice. However, in the remainder in which the capsule or the pelvis is torn, operation will be necessary and, if deferred too long, may not save the patient. Reported statistics indicate that 20 to 30 per cent will require surgery (Just, Lewis and Trimble, Prather, Peacock). The indications for operation are gross infection, persistent hematuria, evidence of urinary extravasation, and loss of renal function. Intravenous urography will help determine the extent of damage to the kidney and in doubtful cases may confirm the necessity for operation. Retrograde pyelography should be resorted to with extreme caution and only when indications for operation cannot be determined by other means; Peacock observed a fatal secondary hemorrhage following this procedure.

Suture of the kidney will usually suffice, but nephrectomy will at times be necessary. The recorded mortality varies from 16 to 30 per cent depending upon the frequency of multiple associated lesions and upon delay in operation in those cases requiring surgery.

Intestine. Early operation after treatment of any initial shock is imperative in intestinal rupture and preferably should take place within 6 hours of the accident. Mortality mounts rapidly with delay beyond that period. Therefore, close and frequent observation and re-examination of doubtful or suspicious cases during *this interval particularly* are obligatory.

Spinal anesthesia facilitates the operative procedure which should be carried out as gently and as rapidly as possible. Suture of the laceration is usually sufficient, this is best done transversely rather than longi-

tudinally (to the long axis of the bowel). With multiple lacerations or extensive mesenteric laceration resection may be necessary. In desperate cases and particularly in large intestinal rupture, obstructive resection, exteriorization, or colostomy may be advisable. Sulfanilamide or sulfathiazole may be used locally in the peritoneum and routinely parenterally as part of the postoperative therapy.

The reported mortality is extraordinarily high. Most recent statistics cite a 60 to 10 per cent rate (Petry, Beitler, Lewis, Estes, Just). Of 1476 cases recently collected by Poer from the literature, the total mortality was 72.1 per cent and the postoperative mortality in 1014 was 59.5 per cent. This may be ascribed to peritonitis, delayed operation, large and multiple lacerations, extensive hemorrhage, and to associated injuries, particularly laceration of the mesentery. Early diagnosis and early operation should tend to lower what would seem to be an unnecessarily high mortality.

Bladder. In rupture of the bladder suture of the rent in its wall, control of hemorrhage, and drainage of the area of extravasated urine will be necessary. The rupture may be intraperitoneal or extraperitoneal, and diagnosis will be facilitated by either intravenous urography or retrograde cystography. Fracture of the pelvis is frequently a concomitant lesion; care of the bladder tear will not interfere with its appropriate treatment. Postoperative sulfanilamide or sulfathiazole therapy will be advisable. The reported mortality ranges from 14.4 per cent (Peacock) to 6.25 per cent (Culver and Baker). It results from other associated severe injuries, massive hemorrhage from laceration of large pelvic blood vessels, and delay in operation (peritonitis). Early recognition of rupture and early operation are imperative.

CONCLUSION

Nonpenetrating trauma to the abdomen may result in an injury that may be treated either by conservative means or operative interference.

Successful treatment depends upon: (1) prompt recognition that an intra-abdominal lesion is present; (2) prompt decision that an operation is necessary; (3) the correct time for and method of operation; (4) the magnitude of the injury.

Clinically, the cases may be classified into three groups: (1) Severe multiple injuries which are rapidly fatal and for which no treatment is of avail; (2) cases that obviously require immediate operation; (3) cases in which the diagnosis is doubtful and the indications for or against operation are not clear.

The history, careful physical examination, repeated blood counts, blood specific gravity and blood protein determinations, urine examination, and roentgenography of the abdomen should be helpful in establishing the diagnosis. In doubtful cases only by frequent repeated re-examination (30 minute intervals) will the developing evidence of a serious lesion be recognized in time to suggest operation before it is too late. Every case of abdominal trauma, therefore, no matter how apparently slight, should be kept under close observation until a sufficient interval has elapsed to determine whether an operation is indicated or not, or until recovery is assured. Lesions of the hollow viscera will demand early operation. Solid visceral injuries, unless accompanied by persistent and unrestricted hemorrhage may more properly be considered candidates for delayed or late operation. Only by close constant supervision and the prompt recognition of an intra-abdominal catastrophe demanding operation can the extraordinarily high mortality in abdominal injury be lowered.

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GUNSHOT WOUNDS OF THE ABDOMEN

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THE general category of gunshot wounds of the abdomen now includes not only injuries due to bullets fired from rifles, revolvers, or machine guns, but those wounds peculiar to warfare which are caused by fragments of shells, bombs, and hand grenades, as well as the "blast" injuries produced by detonation of high explosives.

The problems involved in the management of abdominal war wounds, as well as the seriousness of such injuries, are summarized in the report of the Medical Department of the United States Army in the World War as follows: "The man with an abdominal wound presents one of the serious problems which the military surgeon has to face. No other group of cases furnishes anything comparable to it in testing the medical resources of an army, or the technical skill of its surgeons."

This review will be limited to a consideration of the modifications of procedure and the recent advances in surgical practice which, in some measure, offset the grave consequences of abdominal wounds due to gunfire.

Collection, transportation, and facilities for early treatment. Improved highways, motor ambulance transportation, and even transfer of casualty cases by airplane, have greatly facilitated the rapid removal of patients to hospitals. The importance of providing an adequate supply of oxygen and of preventing extravasation of intestinal contents due to reduced atmospheric pressure at high altitudes has been discussed by Lovelace, who advocates the use of heated sealed pressure cabin airplanes, equipped with apparatus for the administration of oxygen.

The development of mobile military surgical units has made operative treatment possible within 6, or at most 12, hours after injury has been incurred, thus reducing the number of hopelessly delayed cases. In civil practice, the same improvements in transportation and the greater number of well equipped hospitals in small communities likewise permit more adequate and prompt treatment.

Methods for reducing the incidence and seriousness of wounds due to gunfire. The value of body armor as a means of deflecting bullets or of arresting projectiles which are travelling at such a low velocity that they would ordinarily be retained is manifest. The arguments which have been advanced for and against this method of protection, as well as a detailed discussion of various materials and designs for armor, are included in a previous report by Storck. The demonstration by Zuckerman that body ensheathment is protective against "blast" injuries coupled with the fact that body armor has been successfully used in the present European war establish the value of this preventive measure.

The possibility of reducing the severity of peritonitis caused by penetrating wounds of the abdomen through alteration of the intestinal flora by replacement with nonpathogenic bacteria, or by sterilization of the bowel contents through administration of intestinal antiseptics, has been considered in a previous communication by the present author (12). The efficacy of tetanus toxoid immunization has been proved and this simple expedient may be depended upon to avert the deaths which occur among patients with abdominal gunshot wounds who would have survived the visceral lesions alone.

Improved methods of study and estimation of the status of patients with known or suspected abdominal injuries. The duration and degree of shock and hemorrhage often determine the outcome in patients with gunshot wounds of the abdomen, and these factors are of paramount importance both in the selection of cases requiring operative intervention and in the timing of operation. Earlier detection of the existence and progress of shock and hemorrhage is now possible by combining the meth-

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ods presently available for revealing changes in blood concentration, with the older methods for the study of these conditions. Determination of blood specific gravity by means of the falling drop apparatus and estimation of mean corpuscular volume are simple and quick procedures which permit prompt recognition of the presence of, or fluctuations in, the degree of shock and hemorrhage.

Peritoneoscopy, although inadequate for determining definitely whether or not visceral perforation has occurred, may avert unnecessary laparotomy or, on the other hand, may indicate a need for abdominal exploration not revealed by other methods of examination. If proper technical precautions are observed, the finding of hemoperitoneum is evidence of penetration of the abdominal wall.

Intravenous pyeloureterography and retrograde cystography make possible more accurate visualization of presence or extent of injuries to kidneys, ureters, and bladder.

Treatment of shock and hemorrhage. The evolution of methods for preserving and administering whole blood and liquid or dried plasma, along with the development of more accurate means of determining the degree and progress of shock and hemorrhage, have in no type of surgical cases been of greater benefit than to patients with gunshot wounds of the abdomen. There are prospects that the supplies of blood elements available for use in emergencies will be further augmented through the isolation of bovine serum albumen suitable for treatment of shock and hemorrhage in the human.

Observations reported by Kekwick, Marriott, Maycock, and Whitby indicate that plasma and whole blood are equally effective for restoring blood volume, and that with large transfusions only 1 pint in each 3 pints of plasma and blood administered need be whole blood. As a rule, in secondary shock, a rise of from 10 to 20 millimeters of mercury can be anticipated from every 540 cubic centimeters of blood transfused, provided that bleeding has ceased and that no other causes of loss of circulatory fluid are operating. Differentiation is to be made between primary shock due to psychogenic and neurogenic influences from which recovery rapidly occurs following rest and the administration of morphine; and secondary shock, which is indicated by a persistence of systolic blood pressure below 100 millimeters of mercury even after 1 hour of treatment by simple measures, and in which transfusion is necessary. Practically complete replacement of lost fluid is required, and at least half of this should be protein fluid, as otherwise the restoration of blood pressure will be only temporary. Transfusions of as much as 3,000 cubic centimeters within a few hours following injury may be required to afford the full benefit attainable by this type of therapy.

The demonstration by Schnedorf and Orr of the value of oxygen therapy in controlling shock has added to the presently available methods for treating this frequent concomitant condition of gunshot wounds of the abdomen. The evidences advanced by Scudder, Besser, and others of the efficacy of adrenal cortex extract, as well as the observations of Best and Solandt concerning the beneficial effects of pituitary extract and concentrated serum in combatting shock, indicate that these forms of therapy are of definite value.

The thrombin preparation, which Smith and his co-workers have found to be so effective in arresting hemorrhage when topically applied, meets the need for the control of bleeding from liver lacerations when hemostasis by other means is difficult or impossible.

Management of ileus and peritonitis. By the very nature of the wounds and the operative manipulation necessary for their repair, gunshot injuries of the abdomen are inevitably accompanied by some degree of ileus and usually by more or less diffuse peritonitis.

Attempts to remove contaminating material from the peritoneal cavity by lavage are not only futile, but actually increase the extent of infection and add to already existing shock. The impossibility of effectively draining the peritoneal cavity even by the introduction of multiple drains, and the danger of intestinal obstruction due to the presence of drains are now generally recognized. The notoriously poor results obtained by performing enterostomy for the purpose of preventing or relieving ileus are in sharp contrast to the usually satisfactory control of this condition by doses of

morphine sufficient to maintain intestinal tone and by the use of the Miller-Abbott tube, in conjunction, if necessary, with the administration of oxygen for the removal of nitrogen from the intestine, as suggested by Fine, Banks, and Hermanson. The report by Fine, Hurwitz, and Mark concerning the serum content of the fluid present in the lumen of distended loops of bowel and the resulting depletion of plasma proteins in the circulating blood emphasizes the importance of plasma transfusion as a rational part of the therapy of ileus. Degeneration of the adrenal cortex as a result of both ileus and peritonitis occurs so constantly as to imply the need for the administration of adrenal cortical hormone or desoxycorticosterone acetate in the treatment of either or both of these conditions.

Evidences of the efficacy of sulfonamide drugs, both introduced directly into the peritoneal cavity and given parenterally, in preventing or reducing the severity of peritonitis are so numerous and convincing as to leave little doubt that these drugs should be used when peritoneal contamination has occurred.

Penicillin, the bacteriostatic fungus extract which has been the subject of a report by Florey and his associates, and gramicidin, an antibacterial substance obtained from sporulating bacilli and described by Dubos and Hotchkiss, are not rendered ineffective by the para-aminobenzoic acid present in inflammatory processes, and give promise of being useful in the treatment of infections which do not respond to the sulfonamide drugs.

Prevention and treatment of wound infection and wound rupture. The morbidity and mortality in gunshot wounds of the abdomen, due to wound rupture, are lessened by supplementing épluchage and closure of wounds by means of nonabsorbable suture materials, with maintenance of normal plasma protein levels and the prevention of avitaminosis. These same measures, particularly when combined with the instillation into contaminated wounds of sulfonamide drugs, zinc peroxide paste, or other oxidizing antiseptics, or with the delayed closure and adequate drainage of such wounds, greatly reduce the incidence of serious wound infections.

Methods for the prevention and treatment of complications. Through the parenteral administration of glucose and lactated Ringer's solutions, blood plasma, amino-acids, and vitamins, serious nutritional deficiencies can be prevented for at least several weeks.

Fatalities due to pulmonary complications can be maintained at a minimum by early mobilization and deep breathing exercises or tracheal aspiration for the prevention of atelectasis, and by prompt treatment of pneumonitis with specific antisera and sulfonamide drugs. The high mortality in gunshot wounds of the abdomen when associated with "sucking" or "blowing" chest wounds can be lessened by immediate relief of tension pneumothorax and by the closure of thoracic wounds either by approximation of wound edges or the application of airtight dressings which prevent paradoxical respiration.

Recognition of the frequency with which subphrenic, subhepatic, cul-de-sac, iliac fossa, perirenal, and miscellaneous other residual abscesses occur, and adequate drainage following their early detection by means of x-ray or physical examination, avert the deaths due to these complications. Retained shell fragments or other foreign bodies present in such areas of suppuration should, as a rule, be removed at the time that drainage is established.

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TREATMENT OF BURNS

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THE problems associated with the treatment of the severely burned patient continue to interest the clinician and the laboratory worker. A review of the literature (14) on burns published during the past 15 years indicates changing ideas and intelligent thinking regarding therapy. A few of the older principles of treatment have been continually emphasized, but as our knowledge of physiology and pathology in relation to the changes occurring in the human body increases, recent advances have been made which develop a more rational basis for therapy (18). The interchange of ideas and experiences, together with the emphasis of certain important points, have developed a better understanding of the problem. There can be no outline of treatment for general use, as each burned patient deserves individual consideration. A résumé of our present form of management of the severe burn is presented together with a discussion of some of the many ideas advanced relative to present day treatment.

Prior to the publication of Davidson's work (10) in 1925 relative to the use of tannic acid, it was the practice of the individual clinician, as well as the various clinics and hospitals, to adhere to a routine founded on the experiences of either the surgeon or the clinic. The results obtained in many instances were assumed to be satisfactory. The statistical studies, however, showed that the results were far from gratifying. The morbidity was prolonged and the mortality was high, varying from 30 to 40 per cent (Table I).

Wells has stated "the introduction of tannic acid by Davidson . . . has revolutionized and, apparently for the first time in history, standardized the treatment of diffuse burns." The use of tannic acid in the treatment of thermal injuries has maintained a well deserved place in the regimen of many surgeons. It is entirely in keeping with general progress in medical science that many changes have developed regarding therapy. However, the basic concept of toxic absorption from the site of a severe burn which led to Davidson's work, although challenged by many, has not in our opinion been satisfactorily disproved. Likewise in many instances, criticism of the tannic acid method of treatment is unjustified due to the failure of the critics to recognize the basic surgical principles underlying this form of therapy.

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FACTORS INFLUENCING THE PROGNOSIS

A combination of factors influences the prognosis for recovery in the case of every severely burned patient. The general care of the patient is of primary importance. Emphasis in recent years has been placed on the therapeutic measures of value in combating the effects of disturbances in general tissue metabolism. It is important to recognize shock and to treat this condition adequately before consideration is given to the local lesion. The extent of the burn bears some relation to the severity of shock but is not to be relied upon, inasmuch as this reaction may accompany burns of a lesser degree. Shock should be treated by the application of heat, the administration of sedatives, and the usual supportive measures. Blood plasma is of definite benefit in the treatment of shock accompanying severe burns (17). Intravenous saline and glucose solutions are essential to prevent anhydremia in second and third degree burns. Hemoconcentration is present early in the case of severe burns, with the red blood cell count, blood nitrogen, and blood sugar elevated, while the blood chlorides are reduced. It is doubtful if hyperglycemia can be explained as due to hemoconcentration, although dehydration will produce an increase in sugar by accelerating glycogenolysis. A

lowered serum protein appearing after a few days indicates the need for a blood transfusion or plasma. Whole blood should also be given later in the course of treatment, if secondary anemia develops.

In the case of the severely burned patient, there is a rapid increase in the hematocrit reading during the first 6 hours. During the following 12 hours there is a gradual increase with very little change later. A study of the blood of a patient with an extensive burn showed that the hematocrit was 71 per cent at the end of the first hour (23), a fact indicating that there has been a loss of approximately half of the plasma volume. It was found that giving the adult 5,000 to 6,000 cubic centimeters of saline solution intravenously during a 24 hour period caused a marked drop in plasma proteins, frequently to the edema level. Similar observations have been reported by others (15, 17). Therefore, it is advisable to utilize glucose solution to combat dehydration, and to limit the use of saline. Intravenous blood plasma decreases the hemoconcentration more effectively, without causing a drop in the plasma proteins. Whole blood given with moderate amounts of saline will tend to prevent a marked drop in plasma proteins, but does not reduce the hematocrit as rapidly as plasma. Burns involving a third or more of the body in the adult are now given 1,000 cubic centimeters of blood plasma and 1,000 to 2,000 cubic centimeters of glucose and saline solutions intravenously in a 24 hour period. The remaining amount of required fluid is given orally.

Saline and glucose solutions temporarily raise the blood pressure and may be given to fortify the patient until blood is available. The temporary action of these agents is due to their rapid elimination by the kidneys; blood on the other hand is retained longer because of its protein content. Of the blood, the serum alone is vital to this action (9). Hospitals with blood banks have serum or plasma available for immediate use.

Underhill, Kapsinow, and Fisk maintain that following a burn, the permeability of the capillaries is in one direction only, namely, from the capillaries to the tissues. If only saline or glucose solutions are available, the administration of adrenal cortex hormone may be of added benefit, as it is claimed to restore and maintain capillary tone. The clinical experiences of Wilson, Rowley, and Gray (26) show favorable results as regards the use of an extract of suprarenal cortex. Satisfactory responses have also been reported with the use of the synthetic analogue desoxycorticosterone acetate (27). Rhoads, Wolff, and Lee conclude from their observations that adrenal cortical extract is of value in the treatment of the fluid shift occurring in patients after severe burns and reduces the amount of plasma which is required to restore the circulation to normal.

There has been some question regarding the changes in blood potassium in the production of the toxic symptoms associated with severe burns. The work of Tenery showed that the whole blood potassium varied directly with the hematocrit changes and the plasma potassium findings were not important. The plasma potassium levels are usually increased during the first 48 hours. In the patients studied the potassium did not reach a toxic level. Toxic symptoms of burns were present without the presence of a toxic potassium level. Scudder found in a study of plasma potassium in 6 cases with severe burns an elevation similar to those he found in other forms of shock.

TABLE I.—COMPARATIVE MORTALITY WITH TANNIC ACID AND OTHER METHODS[1]

Author	Other methods		Tannic acid	
	No. of patients	Mortality per cent	No. of patients	Mortality per cent
Bancroft and Rogers (New York)	90	40.0	114	20.0
Beekman (New York)	320	37.8	114	14.9
Wilson (Edinborough)	300	38.7	117	11.1
Harris (Toronto)		26.6		12.0
Mason (Philadelphia)	91	28.5	87	13.3
Langer (Vienna)	86	16.3	65	7.7
Mitchiner (London)	243	9.4	249	2.4
McClure and Allen (Detroit)	118	9.3	358	11.7
Glover (Cleveland)	121	14.0	809	8.4
Total patients	1369		1913	
Average mortality		24.5		11.3

[1]From DONALD M. GLOVER and ARNOLD F. SYDOW. Am. J. Surg., 1941, 51: 601.

TABLE II.—REPORTED CAUSES OF BURNS TAKEN FROM THE HOSPITAL RECORDS 1922–1940[1]

Causes	No. of cases	Per cent
Hot fluids (spilling hot liquids from table or stove, stepping or falling in hot water)	563	55.3
Fire (bonfire, stove, gas heater, gasoline, etc.)	263	25.8
Fire (result of playing with matches)	68	6.7
Chemicals	40	3.9
Not stated	84	8.3
Total	1018	
Considered avoidable	820	80.5
Considered unavoidable	114	11.3
Not stated	84	8.2
Total	1018	

[1]From the Children's Hospital of Michigan.

SURGICAL MANAGEMENT

An extensive burn lesion may be compared to a large open wound and deserves rigid aseptic surgical care. The importance of thorough cleansing, combined with débridement of the involved skin areas, cannot be too strongly emphasized. This includes the removal of all foreign material and necrotic tissue, the opening of blebs and blisters, and the removal of loose skin, together with gentle but complete cleansing of the involved surfaces with saline and boric acid solutions. The use of green soap and solvents, such as ether and alcohol, may be necessary. The burn resulting from acid or an alkali should always be thoroughly washed with water before the neutralizing agent is applied (11). Sodium bicarbonate solution is effective in acid burns, and acetic acid may be used as the neutralizing agent in burns from alkalies. In most instances the proper preparation of the burned area may be successfully carried out with little pain by the use of sedatives, such as codeine in the case of young children and morphine in older individuals. Light anesthesia may be required if the procedure necessary to prepare the involved area causes severe pain. Sodium pentathal administered intravenously by a competent anesthetist provides a satisfactory type of anesthesia for the preparation of extensive burned surfaces. (Table II.)

Failure to adhere to the basic surgical procedures in the preparation of the burned area, either because of lack of familiarity with their importance, or because of existing conditions as met with in war zones, has led to adverse criticism of the tannic acid method used in the treatment of the diffuse burns seen in civil life. In peacetime, casualties are usually hospitalized within a short time, but under war conditions many days may elapse before the patient is given proper care (12). This in our opinion has been the chief factor accounting for the disappointing results of the tannic acid treatment of burns in modern warfare.

TOXEMIA OF BURNS

The factors involved in the development of the toxemia which accompanies severe and extensive burns have been widely discussed. Uniformity of opinion on this question is lacking. That infection may be responsible in many cases seems probable. On the basis of bacterial invasion of the local lesion together with the presence of concurrent infections in many young patients, we instituted chemotherapy in 1939 (18). In our first patients sulfapyridine was given orally and when sulfathiazole became available, this drug was substituted because of claims of decreased toxicity. In the absence of any accepted contraindications, chemotherapy is instituted when the temperature reaches 102 degrees F. The dosage in the case of children is calculated on the basis of weight. A total of 1¼ grains per pound of weight is given in the 24 hour period in divided doses at 4 or 5 hour intervals. In the case of adults 1 gram is given every 4 hours. The dosage is then governed by frequent blood level determinations. A level near 4 milligrams per 100 cubic centimeters is desirable. Close clinical observations for complications or unfavorable reactions are necessary, and frequent blood and urine studies are advisable. A favorable clinical response with a decline in temperature is usually apparent in a few hours. There have been no deaths or serious reactions in approximately 75 severely burned patients treated to date by the addition of chemotherapy.

LOCAL USE OF SULFONAMIDE DERIVATIVES

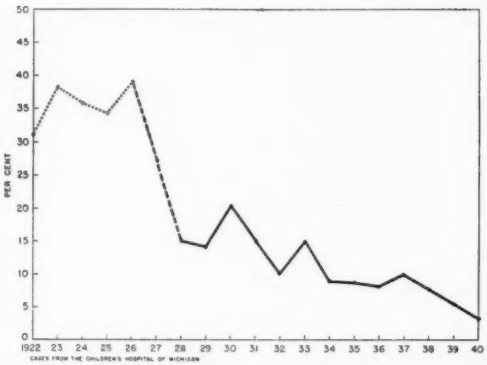
In recent months the suggested use of certain sulfonamide derivatives as a local treatment for cutaneous burns has been proposed. This form of therapy may aid in the preven-

tion of local infection or retard bacterial invasion. Also, since the drug is absorbed, beneficial effects in the case of septicemia may be apparent. Our experience with this form of therapy is limited to an experimental study of a small group of patients treated locally with the sodium salt of sulfathiazole in a water soluble ointment base. Several patients with burns approximating 20 per cent of the total body surface have been treated and responded favorably with the formation of a dry crust, which remained intact and allowed healing without evidence of infection. We believe, however, that this form of therapy is not without certain danger. The rate of absorption is not controlled and high blood levels may occur, particularly in patients with a diminished urinary output. The formation of acetylsulfathiazole crystals in the pelvis of the kidneys and in the ureters may likewise cause serious symptoms due to obstruction. This occurred in one case in our series. Basing an opinion on our limited experience, we believe further experimental study is indicated, together with wider clinical use before local application of the sulfonamide derivatives can be generally recommended. Pickrell has recently advocated spraying cutaneous burns with a 3 per cent solution of sulfadiazine in 8 per cent triethanolamine with satisfactory results in over one hundred cases.

TANNIC ACID

The details of the tannic acid treatment have been outlined in previously published papers (4, 13, 14, 16, 18, 22), but certain important features of this form of therapy deserve repetition. The use of the freshly prepared aqueous solution of tannic acid in 5 per cent strength as a coagulant of the protein on the surface of a burned area has stood the test of time. The application by spraying has been successful and is still popular. Prepared jellies or pastes of 5 per cent or 10 per cent tannic acid strength may be substituted when the freshly prepared solution is not available.

The technique proposed by Bettman (5, 6) combines the use of a solution of 10 per cent silver nitrate and a 5 per cent tannic acid solution. The tannic acid is applied either as a spray or in jelly form, followed shortly by the application of the silver nitrate solution. The claims for this technique, as stated by Bettman, have been substantiated, and we believe that this adjunct to the original tannic acid treatment has proved of distinct value.



Graph. 1. Mortality curve. . . . before use of tannic acid treatment; - - - experimental period; ——tannic acid and gentian violet combined with silver nitrate (10 per cent). Total cases 1,018.

GENTIAN VIOLET

Gentian violet in a 1 per cent aqueous solution as advocated by Aldrich (1) is preferred in burns showing evidence of infection when first seen, or in cases of more than forty-eight hours' duration when first treated. Burns involving the perineum, the hands and feet, and deep burns encircling the extremities or in the region of joints should be treated with gentian violet solution. The coagulum produced by gentian violet is more pliable and obviates splitting of the protective coating over joint areas and permits increased freedom of the hands and feet. The dye may also be combined in the treatment, after the use of tannic acid, when there is separation and evidence of infection about the edges of the coagulum.

GENTIAN VIOLET AND SILVER NITRATE

Following the experience with silver nitrate combined with tannic acid, a similar technique was used, gentian violet being substituted for tannic acid. The results in a small series of cases were satisfactory and provided the basis for a published report (8). This combination has to some extent offset certain disadvantages of the gentian violet solution when used

alone. A firmer coagulum is produced, drying is more rapid, and the disagreeable staining properties are somewhat limited. In addition, the antiseptic properties of the gentian violet solution appear to be increased by the combination with silver nitrate. Aldrich (2) at present advocates the use of a triple dye preparation, namely, crystal violet, brilliant green, and neutral acriflavine for the purpose of a more complete antiseptic action. We have had no experience with this combination.

BURNS OF HANDS AND FACE

Allen has re-emphasized and called attention to the value of aseptic surgical preparation of burns of the hand. Following thorough cleansing of the burned area, the entire surface is covered with a nonadherent type of dressing, such as petrolatum gauze. A voluminous soft dressing is then applied and bandaged to exert pressure to all parts involved, thus minimizing edema and the loss of tissue fluid. The part is then splinted in the position of function. Fourteen days later the original dressing is removed and the less seriously burned areas are usually found healed. Burns of the face deserve special consideration and should not be treated by any stereotype method. Tannic acid jelly may be used effectively for certain burns of this type, but in other instances it may be of advantage to apply saline compresses or Blair's jelly (7), together with the application of pressure.

LATER TREATMENT

The details of the treatment following the separation of the tannic acid or gentian violet coagulum have been previously published (18). However, emphasis should again be placed on the value of early skin grafting. Early grafting of extensive granulating surfaces has saved many lives and should be resorted to as soon as the local lesion is sufficiently prepared to assure successful results. This practice has also aided in minimizing scarring and deformity in many instances. (Graph 1.)

CONCLUSIONS

1. It is important that careful attention be given to the treatment of shock accompanying the diffuse burn.

2. Surgical preparation of the burned area should be performed with the most rigid aseptic technique.

3. The choice of local treatment depends on the location of the burn and the time that has elapsed before therapy is instituted.

4. The maintenance of the fluid and the electrolytic balance, as well as attention to the nutrition of the patient is essential.

5. Measures must be taken to combat infection with the addition of chemotherapy.

6. Early skin grafting minimizes the loss of fluid from the burned area, prevents the development of chronic infection, and aids in limiting scarring and contractures.

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SOME PROBLEMS CONCERNING ACTIVE IMMUNIZATION AGAINST TETANUS

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THE present war and the consequent mobilization of millions of soldiers throughout the world have given a great impetus to the use of toxoid in active immunization against tetanus. Formerly the medical profession in general, with the notable exception of the French, had been rather indifferent to its possibilities. Protection against tetanus, however, is not only a necessary measure in time of war. Infrequent as it is in peace, tetanus is still common enough to be a matter of grave concern, especially in view of the fact that the mortality, though reduced somewhat in recent years by a better understanding of the pathogenesis and treatment of the disease, is still alarmingly high.

Although prophylactic passive immunization with antitoxin has proved very helpful, no one will deny that it leaves much to be desired. One is interminably confronted with the question whether antitoxin should be given in a particular instance. No means of properly determining this issue is available. Anyone who has been called upon to treat tetanus which has resulted from some trivial and apparently clean laceration or abrasion will know forever that it is not only deep contused and punctured wounds incurred in the street or the barnyard that may harbor actively growing Clostridium tetani. Tetanus not infrequently has followed an injury so inconspicuous that no doctor has been consulted; indeed, cases are sometimes seen in which no portal of entry can be demonstrated and in which, naturally, no prophylactic antitoxin has been given. Passive immunization is imperfect also because of the transient character of the protection afforded. The fall in titer after the first week or 10 days necessitates reimmunization after this interval in all cases of persistent infection and in all of those in which manipulation or exploration must be carried out again. Even such precautions fail in those cases of latent toxemia in which the organisms have been growing unobtrusively in apparently clean and healing wounds. The usual dose may be insufficient in case of overwhelming infection. Finally, there is the question of sensitivity, a matter of great concern both in hazard to the patient and in disability and loss of time from work. It is all the more a problem because of the fact that large groups of persons requiring treatment for injuries are notoriously apt to incur other injuries necessitating subsequent injections of antitoxin; for example, industrial workers and children. In addition, there are the matters of expense and difficulty of storage and transportation. Furthermore, the modern method of warfare with its extreme mobility and lack of any fixed line of battle renders the prompt administration of antitoxin to all wounded a matter of almost unsurmountable difficulty. Obviously a more permanent active immunity which can be brought about prior to the time of injury and by a method relatively free of reactions offers many advantages.

A great deal has been learned about tetanus toxoid and the immunity it confers since Ramon and his associates demonstrated that toxin could be completely detoxified and still retain its antigenic properties and that it could be applied to clinical use (7, 34).

Two types of toxoid are available, plain and alum-precipitated toxoid. When the antigenicity of the two has been compared by individual workers the alum-precipitated toxoid has been found to produce a better antitoxin response (9, 15, 18, 29). Nevertheless, techniques have been worked out with

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both types of toxoid which result in an apparently satisfactory production of antitoxin in the injected patient. A single injection of toxoid ordinarily causes no demonstrable production of a significant amount of antitoxin in human subjects (34). The first dose appears to sensitize or prepare the patient so that he will respond to subsequent injections by a rapid and pronounced production of antitoxin. Within 2 weeks after a second and within a week after a subsequent injection, the antitoxin titer rises to an almost certainly protective level (10). It is generally agreed that a relatively long interval is preferable between the two or three doses constituting the basic course of immunization. The recommended interval varies from 3 weeks to 3 months (2, 4, 10, 16, 19, 23, 26).

In addition to the type of toxoid, the number of injections, and the interval between them, the amount and antigenicity of the toxoid are important in regard to the resultant titer. In Table I are listed the antitoxin titers of guinea-pigs at varying intervals after the injection of 1.0, 0.1, and 0.01 cubic centimeter of a commercial alum-precipitated toxoid.[1] It is apparent that the antitoxin response varies according to the amount of toxoid given. These findings are in accord with the observations of others. Gold (11) in human beings, and Sneath (30) and Trabattoni (31) in guinea pigs obtained results suggesting that the antitoxin response is greater with larger doses of toxoid. Von Eisler and Gottdenker concluded from experiments with guinea pigs that the quantity of antigen is more important with reference to the intensity of the antitoxin response from tetanus toxoid than is the case with diphtheria toxoid. Bergey and Etris thought their experiments suggested that antigenicity of toxoid is proportional to the toxicity of the toxin from which it is made. Zoeller and Ramon believed that antigenicity can be estimated from flocculation tests of the toxoid.

[1]The experiments recorded in Tables I, II, and III were carried out in the following manner: Guinea pigs weighing approximately 500 grams were injected subcutaneously with 1.0, 0.1, and 0.01 cubic centimeter of alum-precipitated toxoid. Blood was withdrawn after 1, 3, 4, and 6½ months and each specimen was assayed for antitoxin in the usual manner on guinea pigs, the U. S. government standard test toxin and antitoxin being used. Some of the animals were given varying amounts of a freshly assayed tetanus toxin filtrate in order to ascertain the degree of protection afforded, the toxin injection always being preceded by withdrawal of blood for estimation of antitoxin titer.

TABLE I.—EFFECT OF VARYING AMOUNTS OF TOXOID GIVEN AS A SINGLE INJECTION ON ANTITOXIN PRODUCTION IN GUINEA PIGS*

Amount of toxoid in c.c.	Antitoxin titer in American units per c.c. serum at intervals after administration of toxoid		
	1 month	3 months	4 months
1.0	0.5, 0.5, 0.5–1.0, 1.0, 2.0, 2.0+	3.0, 3.0, 4.0+, >4.0, >4.0	1.0, 1.0, 1.0–2.0, 1.0–2.0, 2.0, 2.0+
0.1	<0.1, 0.1, 0.2–0.25		0.05, 0.1–0.5, 0.1–0.5, 0.1–0.5, 0.1–0.5, >0.5, >0.5
0.01	<0.01, <0.01, 0.1, 0.1+, 0.1+, 0.1+	<0.01, <0.01, <0.01, <0.01, 0.01, 0.05+, >0.05	

*Each figure represents an assay on an individual animal.
In this table and in Tables II and III < indicates an indeterminate amount less than the figure given which represents the smallest unitage at which the serum was assayed; > an indeterminate amount greater than that figure cited.
When a value is followed by +, it indicates that the titer was slightly or moderately higher than the figure cited as evidenced by the condition of the test animals at the end of the period of observation.

These considerations may be of the utmost importance. It is entirely within the realm of possibility, I think, to produce tetanus toxin of such great toxicity that the toxoid made from it will evoke a much great immunity and one of much longer duration. Indeed, it is by no means certain that a single injection of such a potent toxoid may not bring about an antitoxin response in human subjects. One cubic centimeter of the commercial toxoids available will evoke a titer of several units in the guinea pig. Perhaps there is no fundamental difference in the reactivity of men, the usual failure to cause a demonstrable antitoxin production with a single injection being simply a matter of too small a dose or, to put it in a different way, of insufficient antigenicity. A comparable dose in the average adult to that given guinea pigs would be from around 120 to 150 cubic centimeters of the available toxoids. Although workers have almost universally noted no antitoxin in the serum of human beings given one dose of toxoid, there are exceptions. Bergey (2) noted from 0.001 to 0.04 unit of antitoxin per cubic centimeter in 32 persons tested 90 days after a single dose of alum-precipitated toxoid; Marvell and Parish found from 0.005 to 0.01 unit several months after a single dose of alum toxoid; and McBryde found after one injection of alum toxoid that 81.5 per cent of 92

children had 0.01 unit, 14 per cent 0.1 unit and 2.2 per cent 0.25 unit, only 2 children having less than 0.01 unit. Whether McBryde's finding of larger amounts of antitoxin in children is linked with the proportionately larger amount of toxoid per unit of body weight which they received as compared with adults on whom most of these studies have been made, is a matter to be considered.

There is no simple method of testing immunity against tetanus in man, the only method at our disposal being the bio-assay in laboratory animals of the blood serum for antitoxin. One would like to know what titer level is necessary for adequate protection. Ramon (26) was of the opinion that 0.001 international unit represented a protective level in man because horses, which he feels are of the same order of sensitivity, survive the introduction of a splinter infected with a lethal dose of spores when their serum contains this amount of antitoxin. Sneath, Kerslake, and Scruby (29) suggested that 0.01 unit per cubic centimeter is the protective level in man since this titer in guinea pigs affords protection against a lethal spore dose. Cowles concluded from antitoxin titers in man following injection of 1,500 units of antitoxin, and in guinea pigs and mice at the time of infection with spores, that 0.1 or 0.2 unit can give a fairly certain protection. Gold (12) was of the opinion that we should aim at 0.1 unit or more in active immunization because of his antitoxin estimations in subjects given 1,500 units of antitoxin. Since it is impossible to be certain what antitoxin titer constitutes a protective level, it is also impossible to state with certainty how long immunity lasts after a basic course of immunization. Numerous authors have shown appreciable amounts of antitoxin to be present months or years after a course of immunization. Gold (10) found 0.1 unit or more in 92 per cent of subjects 3 months after two injections of alum-precipitated toxoid, 71 per cent in 6 months, 56 per cent in 1 year, 30 per cent in 2 years.

The question has indeed been raised whether antitoxin titer *per se* is in reality a true index of the degree of immunity. Numerous authors have confirmed Ramon's observation that immunized subjects will respond to a subsequent injection with a prompt rise in antitoxin titer. Analyzing reported blood serum titrations on 300 individuals after such "repeat" injections, I find that in 1 week all had 0.01 unit or more, all save 9 had 0.1 unit or more, 204 had 0.5 unit or more. There is no doubt that this capacity of the actively immunized subject to respond quickly to a repeat dose of toxoid is a most important consideration in the efficacy of toxoid as an immunizing agent.

TABLE II.—EFFECT OF A SINGLE NONFATAL DOSE OF TOXIN ON THE ANTITOXIN TITER OF GUINEA PIGS WHICH HAD BEEN GIVEN A SINGLE INJECTION OF TOXOID ONE MONTH PREVIOUSLY*

Amount toxoid in c.c.	Toxin given 1 month after toxoid	Antitoxin titer in American units per c.c. of serum at intervals after injection of toxoid		
		3 months	4 months	6.5 months
1.0	No	3.0, 3.0, 4.0+, >4.0, >4.0	1.0, 1.0, 1.0–2.0, 1.0–2.0, 2.0, 2.0+	
	Yes	>4.0, >4.0, >4.0, >10.0		5.0–10.0, 10.0–15.0, >15.0
0.1	No		0.5, 0.1–0.5, 0.1–0.5, 0.1–0.5, 0.1–0.5, >0.5, >0.5	
	Yes	>1.0, >1.0, >1.0		>10.0, 10.0–20.0, 20.0–50.0
0.01	No	<0.01, <0.01, <0.01, <0.01, 0.01, 0.05+, >0.05		<0.05
	Yes	>0.05		>0.1, >0.1

*The amounts of toxin administered varied as can be seen in Table III.

It is important to know whether the toxin produced in the course of the natural disease will similarly serve to cause a prompt elevation of the antitoxin titer in immunized subjects. It has been known for some time that large doses of toxin are antigenic in horses, and toxin is used in conjunction with toxoid in the hyperimmunization of horses for the production of commercial antitoxin. Table II illustrates the fact that toxin brings about a decided increase in the titer of immunized guinea pigs. Three months after 1.0 cubic centimeter of toxoid has been given to guinea pigs and 2 months after varying doses of

TABLE III.—RELATIONSHIP BETWEEN SERUM ANTITOXIN TITER AT THE TIME OF INJECTION AND THE PROTECTION AGAINST TETANUS TOXIN*

Antitoxin titer in American units at time of injection	Doses of tetanus toxin in median lethal guinea pig doses from which animals succumbed or survived	
	Survived	Died
<0.01		20 (0.01), 20 (0.01), 50 (0.01), 400 (0.01), 800 (0.01)
0.01–0.1	100 (0.01), 300 (0.01), 2000 (0.1)	100 (0.01), 200 (0.01)
0.1–0.5	50 (0.01-T), 75 (0.01-T), 200 (0.01), 360 (0.1), 8000 (0.1)	36 (0.01), 80 (0.01), 11,500 (0.1), 23,000 (0.1), 57,500 (0.1), 80,500 (0.1)
0.5–1.0	2000 (1.0), 40,000 (1.0)	23,000 (0.1), 80,000 (1.0)
1.0–2.0	20,000 (1.0), 8,000 (0.1)**, 10,000 (0.1)**, 16,000**	27,000 (1.0), 57,500 (1.0), 115,000 (1.0), 230,000 (1.0), 575,000 (1.0)
2.0–3.0	20,000 (1.0), 60,000 (1.0)	80,000 (1.0), 115,000 (1.0), 230,000 (1.0), 345,000 (1.0)
>4.0	10,000 (0.1-T), 20,000 (0.1-T), 30,000 (0.1-T), 40,000 (1.0), 50,000 (1.0-T), 60,000 (1.0), 75,000 (1.0-T), 80,000 (1.0), 100,000 (1.0-T), 100,000 (1.0-T), 120,000 (1.0-T)	

*The figures cited represent the amount of toxin in G-PLD 50 s given; the figures in parentheses indicate the amount of toxoid in c.c. the animal had received.
T designates that in addition to toxoid the animal had received an injection of toxin from which it recovered.
**The titer was >1.0.

toxin, the animals have titers exceeding 4 units per cubic centimeter, whereas 2 of 5 control animals have only 3 units. Although in 4 months the titers of the controls have fallen to 1 or 2 units, those which had received toxin have titers of from 5 to more than 15 units in 6½ months. Results in animals immunized with 0.1 and with 0.01 cubic centimeter of toxoid are similar. Such studies demonstrate that toxin in sufficient but not fatal amounts serves in the course of several months to cause a significant increase in antitoxin titer. They do not, however, answer the question whether this response is rapid enough to increase a low titer to a protective level before the patient might succumb to natural infection with Clostridium tetani. Others have attempted to answer this point with somewhat confusing results.

Jones and Jamieson (20) found that a number of actively immunized guinea pigs survived a lethal spore dose but did not respond with an increase of serum antitoxin, assays being made on the seventh day and in some instances on the second, fourth, and fourteenth days. Jaulmes and Jude similarly found no increase in titer on the third, sixth, and tenth days after immunized guinea pigs had been given a lethal dose of spores from which they all recovered without symptoms. One explanation which leaves open the question of possible titer acceleration is that the toxin is neutralized as formed and has no opportunity of exerting antigenic activity (4, 17). Wolters and Dehmel found that two guinea pigs with low titers survived the introduction of splinters infected with a lethal dose of spores and showed increased titers on the sixth and eighteenth days. Zuger, Greenwald, and Gerber concluded from experiments with guinea pigs that actively immunized animals respond to toxin with increased titers on the fourth and fifth days and to infection with spores with a delayed titer rise, a significant elevation occurring first on the 8th or 10th day. This rise seemed to occur too tardily to afford adequate protection and suggested that such a rise following natural infection in man probably cannot be relied upon to give sufficient protection. Our experiments suggest that the degree of protection against tetanus toxin depends upon the antitoxin titer at the time the toxin is administered (Table III). It appears that any increase in antitoxin which the toxin may have stimulated did not reach a sufficiently high level rapidly enough to alter the outcome, unless such a rise was almost directly proportional to the titer at the time the toxin was administered. This type of study should be extended to include inquiry into the degree of protection afforded by a given antitoxin titer induced by passive immunization as compared with the same titer resulting from active immunization. It should also be determined whether a given antitoxin titer confers the same degree of protection at a time when the titer is rising, at its peak, or on the decrease, as well as whether it resulted from a certain dose of toxoid or from a fraction of this dose. Such studies would throw addi-

tional light upon the question whether there is some immunity conferred by toxoid other than that represented by the antitoxin in the blood. Trabattoni states that immunity may persist in guinea pigs immunized with toxoid even when the serum antitoxin is diminished or absent, which he interprets as indicative of a true tissue immunity.

The general plan of immunization consists of 2 or preferably 3 injections of toxoid given at long intervals, never less than 4 weeks, and a reinjection at the time of injury. In certain instances it may be wise to keep the titer high in advance of possible injury by administration of toxoid at intervals of 6 months or a year. For such purpose the intranasal instillation of refined toxoid (topagen) is satisfactory (13). The French army uses 3 doses of the "triple vaccine" given at 3 week intervals, the British army 2 doses of plain toxoid at 6 week intervals. The United States Army uses 3 injections of plain toxoid 3 or 4 weeks apart, a stimulating dose at the end of the first year, another during the month before departure for the zone of combat unless this takes place within 6 months of the stimulating dose, and another dose at the time of injury. The United States Navy and Marine Corps use a similar plan except that alum-precipitated toxoid is used and the basic course consists of 2 injections 4 weeks apart. The demonstration that the simultaneous injection of tetanus toxoid with diphtheria toxoid or with typhoid-paratyphoid vaccine or with both is not only feasible but actually results in a higher antitoxin titer (19, 21, 27), is an important contribution. Tetanus toxoid can be easily given during the almost universally practiced immunization against diphtheria in infants and may be given advantageously to those being immunized against typhoid fever.

Ramon (26) stated that after thousands of injections no reactions of any moment had occurred. Several anaphylactic reactions in Great Britain have been reported. Cunningham and Parish and Oakley have each reported a case of nonfatal anaphylactic shock. Whittingham stated that among 61,042 members of the Royal Air Force who were immunized, 2 had anaphylactic reactions and 12 constitutional symptoms such as malaise and fever. Seven of these had urticaria. Few reactions have been reported in this country. Jones and Moss (18) noted 2 delayed reactions consisting of local soreness and fever. Hall (15) encountered 2 urticarial reactions with the second dose of plain toxoid. Subsequently (16) he encountered one delayed urticarial reaction and 2 reactions with fever and malaise on the first injection of an alum-precipitated toxoid. On giving the second injection of this toxoid to 1,800 of these persons, 7 had fever and malaise, 4 had urticaria, and 1 had anaphylaxis. The other 500 were given another toxoid which he felt was more carefully washed, with no reactions at all. Gold (14) collected from his own experience and that of other workers 1,700 cases of patients immunized with alum-precipitated toxoid in whom there were only 2 cases of urticaria. No fatal reactions have occurred, and the reported incidence of general reactions of all sorts is surprisingly low in view of the millions of persons who have been immunized. Although there is no general agreement, investigation to date tends to link the reactions to sensitization to the Witte or Berna peptone used in the culture medium in which the organisms were grown. There is reason to have confidence in the production of purer toxin by use of other media and methods of culture from which toxoids may be prepared which will cause no reactions.

The efficacy of tetanus toxoid has been repeatedly demonstrated in laboratory animals. The present armed conflict is putting to crucial test the protection afforded in man by toxoid. Active immunization is compulsory in the French and Italian armies, and is also used in the Russian army. Though on a voluntary basis, a large part of the British army has been actively immunized. I can find a record of only a single instance of tetanus in an actively immunized person, a patient reported by Simon and Patey, who had "an essentially benign and localized form of tetanus" from which he recovered. The campaign in Flanders and the evacuation from Dunkirk gave indisputable evidence of the value of active immunization (1, 25). Ninety per cent of the British Expeditionary

Force were immunized. Each wounded man was to have been given 3,000 units of antitoxin, but because of the force of circumstances the majority of the wounded reached England without having received any antitoxin. Among approximately 1,800 wounded men who were not immunized there were 8 cases of tetanus; there were no cases of tetanus among some 16,000 wounded who had been actively immunized.

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THE CLINICAL SIGNIFICANCE OF THE SERUM AMYLASE TEST IN THE DIAGNOSIS OF ACUTE PANCREATITIS

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IN the last few years a number of clinicians have used determinations of the level of amylase in the blood serum as an aid in the differential diagnosis of acute pancreatitis. This laboratory test has been used on the University of California Emergency Service at the San Francisco Hospital for the last 3½ years and has proved to be of considerable assistance in making a diagnosis of acute pancreatitis. In the differential diagnosis of certain other cases of acute, but obscure, abdominal disease the test has been of value in excluding the possibility of acute pancreatitis.

It is essential that the technique for the determination of serum amylase be standardized, and its accuracy confirmed repeatedly before the results can be considered significant. The normal range of serum amylase levels must be known, and their possible variations must be realized before a correct interpretation of the test can be made. We have used Somogyi's "saccharogenic" method for the determination of amylase as well as his definition of the unit. The amylolytic activity of the serum of any given normal person is usually very nearly at the same level regardless of fasting, feeding, kind of food, time of day, exercise, etc. (Fig. 1). Serum amylase activity in groups of normal persons is reported by most observers as being almost always within the limits of from 80 to 180 units, though Lewison reported from 40 to 175 units as the normal range in his series, and Comfort gave 320 units as the upper limit of normal. In our investigations, variations from the range between 80 and 180 units usually did not occur in normal persons, but occasionally readings below the normal limit (that is below 80 units) were found in those apparently healthy.

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A considerable elevation in serum amylase almost always occurs at some time during an episode of acute pancreatic necrosis, acute interstitial pancreatitis (acute pancreatic edema) or acute traumatic pancreatitis. Significant elevations in the amount of amylase found in the serum rarely occur except in certain phases of acute disease of the pancreas, although in certain instances acute parotitis will cause a rise in serum amylase and occasionally diseases of the kidney are accompanied by a slight elevation resulting from impaired renal excretion. Renal disease with retention of amylase is readily recognized if determinations of both serum and urinary amylase are made in all cases in which the serum amylase is only slightly increased.

In the past 3½ years, 743 amylase determinations have been made on patients on the University of California Service at the San Francisco Hospital. Most of them were made on blood serum in cases of suspected pancreatitis, or in conditions in which differentiation of pancreatitis from other acute abdominal disease was difficult. Other amylase determinations were made on bile, urine, peritoneal fluid, and fluid from cysts. The serum amylase was studied in 43 cases of acute pancreatitis. The lowest maximum reading in any single case of this disease was 225 units, the highest was 2,459 units, and the average maximum reading was 696 units. The average undoubtedly would have been higher had not a number of the patients entered late in the course of their disease when the amylase level was probably subsiding. In 35 of the 43 cases the diagnosis was acute interstitial pancreatitis (acute pancreatic edema), in 6 acute hemorrhagic pancreatitis (acute pancreatic necrosis) was diagnosed, and there were 2 cases of traumatic pancreatitis (Table I).

In more than 200 other cases of acute abdominal disease the serum amylase test was used as a diagnostic aid to rule out the possi-

TABLE I.—CASES OF ACUTE PANCREATITIS STUDIED BY THE SERUM AMYLASE TEST

	No. of cases	Confirmed by operation or autopsy	Deaths
Acute hemorrhagic pancreatitis (Pancreatic necrosis)	6	4	4
Acute interstitial pancreatitis (Pancreatic edema)	35	13	1
Acute traumatic pancreatitis	2	2	0
Total	43	19	5

bility of acute pancreatitis. When the amylase test is done within the first 2 or 3 days of the acute illness, a low or normal reading is of considerable value in eliminating the likelihood of acute pancreatitis.

Determinations of serum amylase were made in 42 cases of acute cholecystitis (Table II). In 14 of the 42, the additional diagnosis of acute pancreatitis was made because of high serum amylase readings and in 8 of the 14 the diagnosis was confirmed by operation or autopsy. Acute pancreatitis was diagnosed in 6 of 26 cases of chronic cholecystitis because of high serum amylase readings (Table II) and in 4 the diagnosis was confirmed at operation or autopsy. Table II shows the serum amylase values found in 12 cases of stone in the common duct. Acute pancreatitis was present in 1 of these in which the amylase level was 1,875 units.

The following case reports are examples of the 3 main types of proved acute pancreatitis that show great elevations in the serum amylase level, namely, pancreatic necrosis, interstitial and traumatic pancreatitis.

CASE 1. A housewife 38 years of age complained of severe epigastric pain radiating to the back, associated with nausea and vomiting of 8 days' duration. There had been no previous attacks and there was no history of alcoholism. She appeared to be acutely ill. The abdomen was distended, there was ecchymosis in the flanks and Cullen's sign was present. A large tender mass was palpated in the epigastrium. The temperature was 102 degrees, the pulse rate 114, and the white blood count 21,000, with 90 per cent polymorphonuclear cells. Urinalysis showed a trace of albumin and slight glycosuria. The *serum amylase* was *1,158 units* on the eighth day of the illness. The icterus index was 32. The patient's temperature ranged between 101 and 103 degrees. On several occasions she developed profound shock associated with cyanosis from which she recovered temporarily following transfusions of blood. On the tenth day of the disease the epigastric mass was drained through a small midline incision, under local anesthesia. A considerable amount of hemorrhagic fluid was found together with necrosis of fat and acute hemorrhagic necrosis of the pancreas. The patient died on the eleventh day. At autopsy acute pancreatic necrosis and fatty degeneration of the liver were found. The gall bladder and bile ducts were normal.

TABLE II.—SERUM AMYLASE IN DISEASE OF THE GALLBLADDER AND BILE DUCTS

Disease	Serum amylase—Units 0–80	80–200	over 200	Total Cases
Acute cholecystitis	16	12	14	42
Chronic cholecystitis	7	15	6	28
Common duct stone	5	6	1	12
Total	28	33	21	82

CASE 2. A housewife 43 years of age had pain in the epigastrium and right upper quadrant of the abdomen, with vomiting of 24 hours' duration. She had had a similar attack 2 weeks previously. There was no history of alcoholism. Tenderness, spasm and rebound tenderness were present throughout the entire abdomen, but were most marked in the right upper quadrant. The temperature was 103 degrees, the pulse rate 104 and the white blood count 21,000, with 98 per cent polymorphonuclear cells. The only abnormal finding on urinalysis was a faint trace of albumin. The level of the serum amylase was not determined at this time. The diagnosis was acute cholecystitis. At operation the gall bladder was found to be normal but the pancreas was indurated and edematous. The *serum amylase* was *262 units* on the first postoperative day. The convalescence was uneventful. Subsequently the patient had numerous episodes of mild abdominal pain. A very severe attack of epigastric pain occurred about 1 year later and, after 24 hours, she entered the hospital again. She appeared acutely ill. The abdomen was tender and spastic throughout with most marked findings in the epigastrium and right upper quadrant. The temperature was 100 degrees, the pulse rate 110 and the white blood count 11,800, with 81 per cent polymorphonuclear cells. Urinalysis showed a faint trace of albumin. The *serum amylase* was *1,105 units* on the first day and *630 units* on the third day. The attack subsided spontaneously.

CASE 3. A boy 9 years of age, hit by an automobile, fell to the street striking his left side, about 1 hour before he entered the hospital. He complained of severe pain in the left upper abdominal quadrant. There was no radiation of pain and no vomiting Tenderness, rebound tenderness, and spasm were present in the left upper abdominal quadrant. The temperature was 98.6 degrees, pulse rate 120, and blood pressure 130/80. A blood count showed 11,900 white blood cells, with 55 per cent polymorphonuclears, 80 per cent hemoglobin, and 4,800,000 red blood cells. During 4 hours' observation, the abdominal findings increased somewhat in severity.

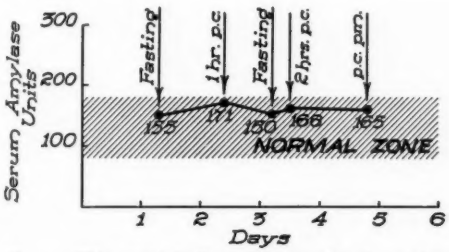

Fig. 1. This graph indicates the results of a series of serum amylase determinations taken on a normal person at various times over a period of 4 days. The readings are very nearly the same regardless of fasting, feeding, time of day, etc. The shaded area designated as "normal zone" represents the usual range of variations of normal serum amylase levels in a group of normal persons.

The *serum amylase* level was *2,117 units*. The diagnosis was traumatic rupture of the spleen and traumatic pancreatitis. At operation, a large amount of bloody fluid was found in the peritoneal cavity. The spleen was found to have been lacerated and was removed. The tail of the pancreas was edematous and hemorrhagic. The patient recovered.

Several types of variations that may occur in the serum amylase level during an episode of acute pancreatitis must likewise be considered. In order to understand these variations a number of patients were studied over a period of several days and serum amylase determinations were made at intervals of from 8 to 12 hours. At the same time, an attempt was made to correlate the clinical course of the acute pancreatic disease with the variations in serum amylase. In this study we noted 6 types of variation of the serum amylase level in acute pancreatitis: (1) sharp rise and fall to normal; (2) sharp rise and fall to subnormal; (3) fluctuations (following the clinical subsidence of acute pancreatitis); (4) sustained high levels; (5) secondary elevations; and (6) slight increases.

In the following discussion a case report is given to illustrate each type.

1. Sharp rise and fall to normal. A sharp rise in serum amylase almost always occurs within a few hours after the onset of acute pancreatic disease, and the level usually remains elevated for from 24 to 72 hours, and then declines sharply into the normal zone (Fig. 2). The height of the rise of the serum amylase level during an episode of acute pancreatitis does not necessarily reflect the severity or indicate the type of the acute pancreatic disease. The declination in the curve does not always correspond exactly to the subsidence of the acute process, but often it does in the acute interstitial type of pancreatitis. Occasionally the level of serum amylolytic activity declines more gradually than usual following an attack of acute pancreatitis. As far as we know at the present time, this latter finding is of no particular significance.

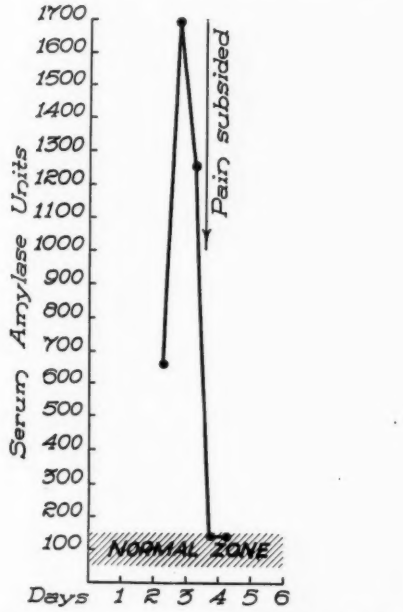

Fig. 2. (Case 4, male, aged 38.) Sharp rise and fall of the serum amylase level in a case of transient acute interstitial pancreatitis associated with acute alcoholism.

CASE 4. A man 38 years of age had been drinking considerable quantities of alcohol for several days before the onset of his illness. For about 48 hours prior to his entry into the hospital he had had severe burning epigastric pain radiating to the back. He vomited once. There had been a similar attack 3 years before. His abdomen was tender throughout with maximum tenderness in the epigastrium and some spasm in the same region. His temperature was 99.6 degrees and pulse rate 68. Urinalysis showed a trace of albumin but no sugar. The white blood count was 26,200 with 89 per cent polymorphonuclear cells. Serum amylase studies were taken twice daily (Fig. 2). The pain and tenderness had subsided completely by the day after entry to the hospital but slight spasm remained in the epigas-

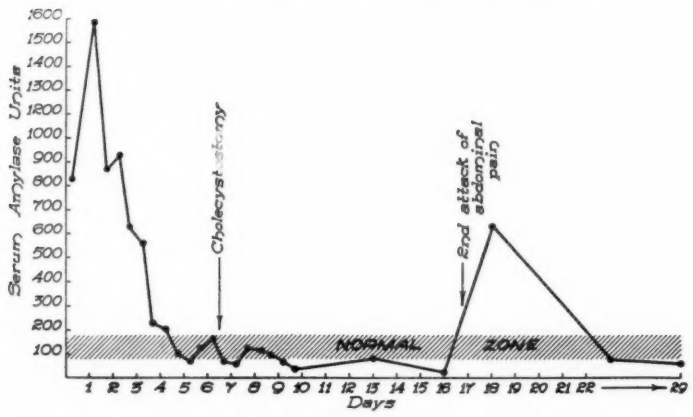

Fig. 3. (Case 5, female, aged 69 years.) Sharp rise and fall into the "subnormal" zone of the serum amylase level in a case of acute cholecystitis and acute pancreatitis. A second attack of abdominal pain on the seventeenth day of hospitalization was accompanied by a second elevation in the serum amylase level.

trium. On the third day the patient had no symptoms or signs of his disease and left the hospital.

2. Sharp rise and fall to subnormal level. The final explanation of the dip below the normal zone that sometimes occurs in acute pancreatitis has not been made, although most observers believe that the extremely low levels correspond to episodes of impairment of hepatic function. The possibility that the normal zone of serum amylase activity should be reduced to include lower readings (below 80 units) must also be considered.

CASE 5. A woman 69 years of age complained of aching pain in the right upper quadrant, radiating to the tip of the right scapula, with nausea and vomiting of 12 hours' duration. She gave a history of chronic cholecystitis with many episodes of colic for 40 years. She was very obese and acutely ill. The abdomen was moderately distended and guarding and tenderness were noted in the epigastrium and right upper quadrant. Her temperature ranged from 100 to 102 degrees and her pulse rate from 90 to 110; the white blood cell count was 18,600. The patient appeared to improve but because of the severe tenderness remaining in the right upper quadrant, acute cholecystitis was suspected. Cholecystostomy was done under local anesthesia. The gall bladder was inflamed and contained calculi. The amylase in the peritoneal fluid was 89.5 units and that in the bile, 170 units. The amylase levels in the blood serum are shown in Figure 3. On the seventeenth day after entry, the patient had a second attack of moderately severe pain and tenderness in the right upper quadrant that subsided within 48 hours. Cholangiography showed a calculus at the lower end of the common duct.

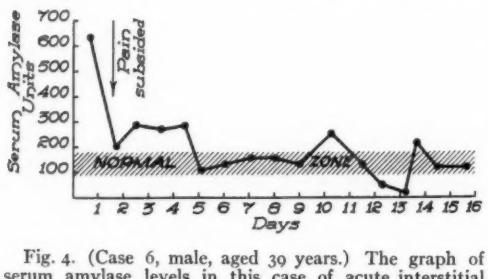

Fig. 4. (Case 6, male, aged 39 years.) The graph of serum amylase levels in this case of acute interstitial pancreatitis associated with acute alcoholism demonstrates the fluctuations above and below, as well as within the usual normal zone, that sometimes occur following the subsidence of an attack of acute pancreatitis.

Case 9 (Fig. 7) also illustrates this fall of the serum amylase level below the normal zone following an attack of acute pancreatitis.

3. Fluctuations within the normal zone and slightly above and below the usual normal range (from 80 to 180 units) occur rather frequently during the days following an episode of acute pancreatitis. At present, the significance of these fluctuations is unknown. The "subnormal" readings mentioned are often a part of this fluctuating curve as may be seen in Figure 4.

CASE 6. A brewer, 39 years of age, gave a history of drinking very large amounts of alcohol for a period

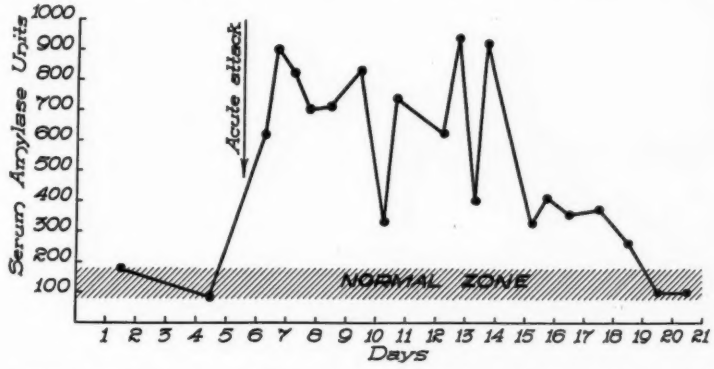

Fig. 5. (Case 7, male, aged 49 years.) Sustained high amylase levels in a case of acute cholecystitis and acute pancreatitis. In this case the serum amylase remained elevated for 4 or 5 days following the subsidence of signs of acute pancreatitis. Sustained high amylase levels are more often associated with a continuation, extension, or progression of acute pancreatitis.

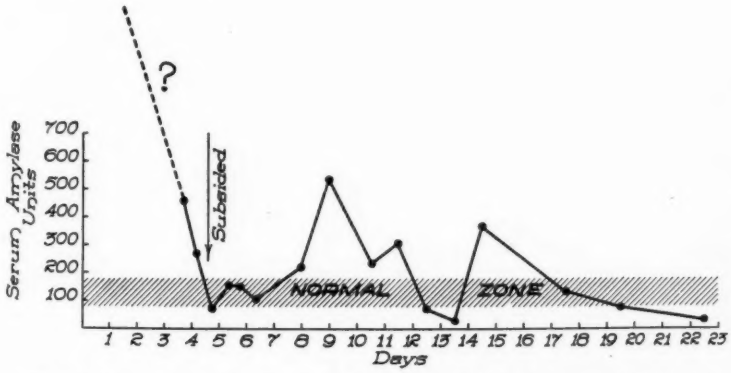

Fig. 6. (Case 8, male, aged 47 years.) Moderately high secondary rise in serum amylase level that developed following the subsidence of the signs and symptoms of an attack of acute pancreatitis. In this case there were no symptoms or signs of exacerbation of acute pancreatitis to correspond to the secondary rises in serum amylase.

of 1 month. He entered the hospital complaining of severe and constant epigastric pain associated with nausea and vomiting of 18 hours' duration. The abdomen was obese and spasm and tenderness were noted in the upper part of the abdomen. The temperature was 101.6 degrees and the pulse rate 116. The white blood count was 17,300, with 80 per cent polymorphonuclear cells. The urinalysis showed a trace of albumin but no sugar. The serum amylase levels are shown in Figure 4. The pain and abdominal findings subsided in 24 hours, but fever and vomiting continued for several more days.

4. Sustained high amylase levels may be associated with a continuation, extension, or progression of acute pancreatitis, or with acute exacerbations of pancreatitis occurring at very frequent intervals. Case 7 demonstrates sustained high amylase values.

Case 7. A man 49 years of age complained of cramping pain which began in the left upper quadrant and radiated to the left shoulder and back. He was nauseated and vomited several times. There was a history of chronic cholecystitis and occasional episodes of severe colic in the left upper quadrant, of 10 years' duration. There was no history of alcoholism. The patient was jaundiced, the abdomen was moderately distended and there was tenderness in the entire upper part of the abdomen, most marked in the epigastrium. The temperature was 98.6 degrees and the pulse rate was 100 on entry. Blood

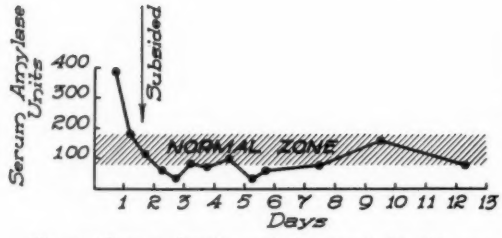

Fig. 7. (Case 9, female, aged 69 years.) In this case in which the clinical signs and symptoms were rather typical of acute pancreatitis, the slight elevation in serum amylase is somewhat confirmatory of acute pancreatitis. This graph also shows the "dip" below the normal zone of serum amylolytic activity that sometimes follows an attack of acute pancreatitis.

count showed 7,600 white blood cells, with 68 per cent polymorphonuclears. The urine contained bile but was otherwise negative. On the morning of the seventh day after entry, the patient had severe pain in the left upper quadrant with nausea, vomiting, and epigastric tenderness. The white blood count was 18,100 and urinalysis showed a heavy trace of albumin. The serum amylase readings are shown in Figure 5. The diagnosis was acute pancreatitis and acute and chronic cholecystitis with icterus. The acute abdominal symptoms and signs subsided over the next 3 days, but the amylase level remained elevated for more than a week and gradually declined into the normal zone (Fig. 5). Operation was performed during a quiescent period. The gall bladder was still somewhat inflamed and edematous and contained many calculi, the common duct was enlarged and contained a large soft stone, and the pancreas was enlarged and indurated.

5. Acute exacerbations of pancreatitis are often reflected in the graphic curves of serum amylase readings as secondary elevations when the patient has had more than one episode of acute pancreatitis while under observation. Case 5 (Fig. 3) serves as an example of a case of acute pancreatitis in which there was an exacerbation of the disease while the patient was in the hospital. Occasionally these secondary rises in the level of serum amylase follow a few days after an attack of acute pancreatitis without subjective or other objective findings indicative of an exacerbation of the disease. After the subsidence of an episode of acute pancreatitis, a rise in the serum amylase, not necessarily accompanied by abdominal pain, may be caused by the manipulation of the pancreas that sometimes occurs during the course of surgical procedures on the bile duct.

CASE 8. A man 47 years of age complained of severe epigastric pain and vomiting of 4 days' duration. He had had no abdominal pain or indigestion previously. He had used alcohol many years before, but none recently. The abdomen was moderately distended and generalized tenderness and spasm were most marked around the umbilicus. The temperature was 100 degrees and the pulse rate 80. The white blood count was 15,400, with 87 per cent polymorphonuclear cells. The urinalysis was negative. The abdominal pain and tenderness subsided over a period of 3 days, and the patient remained free from symptoms thereafter during his hospitalization. The serum amylase level, however, rose to 530 units on the ninth day, though there were no symptoms or signs of disease at that time (Fig. 6). Operation was performed during a quiescent period. Mild chronic cholecystitis and edema and induration of the entire pancreas were found. Cholecystectomy was done.

6. Slight increases in the serum amylase are of relatively less diagnostic value than are the moderate or large increases that usually accompany the early course of acute pancreatitis. Slight elevations in serum amylase, however, may be considered as somewhat more significant when they are found in patients who present themselves late in the course of acute pancreatic disease, or just after the subsidence of a typical episode of acute abdominal pain. Case 9 is illustrative.

CASE 9. A woman 69 years of age complained of severe epigastric pain and vomiting of 24 hours' duration. She had had no abdominal discomfort previously, and there was no history of alcoholism. Marked tenderness was present in the epigastrium. The temperature was 100 degrees and the pulse rate 70. The blood count showed 17,700 white blood cells, with 90 per cent polymorphonuclears. The urine showed a trace of albumin. The pain and tenderness subsided completely over the ensuing 24 hours. The gall bladder visualized normally by cholecystography. Figure 7 shows the serum amylase determinations.

If the clinical picture is less typical of acute pancreatitis, these slightly increased serum amylase readings must be considered equivocal. This is seen in Case 10.

CASE 10. A woman 63 years of age complained of severe pain in the right upper quadrant, with nausea and vomiting of 2 days' duration. She was not particularly ill. Her previous history suggested chronic cholecystitis of many years' duration. She used alcohol occasionally. There was tenderness throughout the entire abdomen, most marked in the upper right quadrant where spasm was also present. The temperature was 99.2 degrees and the pulse rate 72.

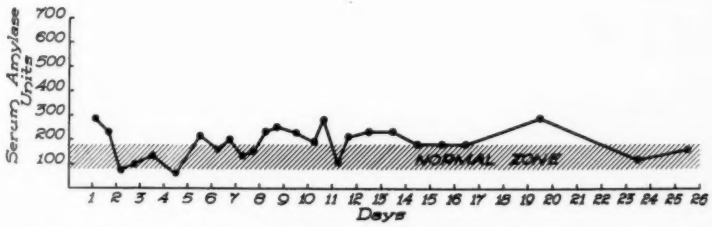

Fig. 8. (Case 10, female, aged 63 years.) The slight elevations in the serum amylase level are of relatively less confirmatory value in this case in which the clinical findings are not typical of acute pancreatitis.

Blood count showed 9,300 white cells with 86 per cent polymorphonuclears. The urine showed a trace of albumin but no sugar. The symptoms and signs of illness subsided over a period of 3 days. The gall bladder was visualized normally by cholecystography. The serum amylase readings are shown in Figure 8.

SUMMARY

The laboratory determination of the serum amylase is a valuable diagnostic test in acute disease of the pancreas. Moderate to marked elevations in serum amylase activity occurring early in the course of an acutely painful abdominal condition offer confirmatory evidence of acute pancreatitis. The serum amylase test is also of some value in the recognition of acute pancreatitis occurring as a complication of cholecystitis or disease of the bile ducts.

The limitations and possible variations of the test for serum amylase must be known before its diagnostic value can be realized. Within these limitations the test may often be of considerable assistance to the surgeon. Six variations that may occur in the serum amylase during, and immediately after, an episode of acute pancreatitis are described.

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THE EFFECT OF DISTENTION OF THE SMALL INTESTINE, ANOXEMIA AND OXYGEN THERAPY UPON THE FLOW OF BILE AND URINE IN THE DOG

Relationship to the Hepatorenal Syndrome

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THERE has been much speculation as to the cause of the combined failure of liver and kidney function and degeneration in some cases of intestinal obstruction, peritonitis, hyperthyroidism, and burns. We have tried, therefore, to investigate the possible existence of a physiological basis for the occurrence of the hepatorenal syndrome in these conditions.

We first studied the effect of distention of the entire small intestine upon the flow of bile and urine. These experiments were performed upon 10 dogs fasted for 18 hours and anesthetized with sodium pentobarbital (30 milligrams per kilogram of body weight intravenously). The blood pressure was recorded from the cannulated left carotid artery. The respiration was recorded from a bellows around the chest of the dog. Bile flow was studied in 7 dogs by cannulating the common bile duct close to the duodenum after ligation of the cystic duct near the common duct. The drops of bile were recorded by an electrical recorder. A ligature was placed around the duodenum and a large cannula was tied into the terminal ileum which was also ligated, distal to the cannula. The cannula was attached to a mercury manometer and an inflation bulb by means of a Y tube. The abdominal wall was closed with heavy silk suture. A control basal flow of bile was then obtained after an interval of about 30 minutes.

Intestinal distention was maintained at pressures of 20, 40, and 70 millimeters of mercury for a period of 30 minutes each. Oxygen was administered by means of a nasal catheter to determine what effect it had upon the bile flow with the intestine distended to pressures amounting to 40 and 70 millimeters of mercury.

The excretion of urine was studied in a similar manner upon 3 dogs. Each ureter was cannulated, and the flow of urine was recorded on a revolving kymograph drum by electrical recorders. A uniform mild diuresis was maintained by the continuous intravenous drip administration of 1000 cubic centimeters of physiologic sodium chloride solution over a period of 4 hours. In all of the experiments, especial care was taken to avoid the kinking of the cannulas when the intestine was distended.

Results. Intraenteric pressures of 20 and 40 millimeters of mercury resulted in a decrease in the bile flow of 7 to 42 per cent below the control level in 6 of the 7 dogs (Table I). Dog 6 showed no change. These pressures are comparable to intraenteric pressures in human cases of intestinal obstruction reported by Wangensteen. Since higher pressures may occur in some clinical cases of intestinal obstruction, we distended the intestine to a pressure of 70 millimeters of mercury and found a further decrease in the bile flow in 4 dogs. Oxygen therapy lessened this inhibition in all of the dogs treated.

Nervous reflex inhibition of the flow of urine did not occur upon distention of the small intestines to pressures of 20, 40, 60, and 90 millimeters of mercury. An increase in the urine flow from 11 to 81 per cent occurred (Table II). This was attributed to an increased blood flow through the kidneys.

The blood pressure in each instance was not significantly altered by distention of the small intestine.

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TABLE I.—EFFECT OF ACUTE INTESTINAL DISTENTION UPON THE FLOW OF BILE IN THE NEMBUTALIZED DOG

Dog No.	Intraenteric pressure in millimeters of mercury				
	20 Per cent	40 Per cent	70 Per cent	70 plus oxygen Per cent	Control after release of pressure Per cent
1	−16	+ 5	+ 5		−16
2	−20	− 6	−26		−36
3	−15	−15	−30		−30
4	−16	−22	−16	− 5	
5	−28	−42	−38	−23	
6	0	0	−15	0	
7	− 7	−14	−42	− 7	0

The depth of respiration was decreased and the rate was increased by distention. Oxygen therapy decreased the respiratory rate and lessened the depression of bile flow produced by distention of the small intestine.

The second part of this investigation was concerned with the effect of anoxemia upon bile and urine flow in 10 nembutalized dogs. The blood pressure, respiration, and the flow of bile and urine were recorded upon each dog as previously described. Mixtures of 5, 10, 15, and 20 per cent oxygen with nitrogen and 100 per cent oxygen were administered by a Heidbrink gas machine. Each mixture was breathed for 30 minutes before and during the time that a tracing was taken. Five per cent oxygen was given as long as the animal could tolerate it. This was usually found to be 5 to 10 minutes.

Results. Inhalation of 15 per cent oxygen in nitrogen for 30 to 45 minutes resulted in a 16

TABLE II.—EFFECT OF ACUTE INTESTINAL DISTENTION UPON THE SECRETION OF URINE IN THE NEMBUTALIZED DOG

Dog No.	Intraenteric pressure in millimeters of mercury				
	20 Per cent	40 Per cent	60 Per cent	90 Per cent	Control after release of pressure Per cent
1	+11	+26	+50	+81	−12
2	+120	+100	+360	+80	+80
3	+57	−18	+12		−14

TABLE III.—EFFECT OF INHALATION OF VARIOUS OXYGEN CONCENTRATIONS UPON THE FLOW OF BILE IN THE NEMBUTALIZED DOG

Dog	Per cent oxygen inhaled for one-half hour			
	15 Per cent	10 Per cent	5 Per cent	100 Per cent
1	−25	−75	−62	0
2	−18	−31	−100	−87
3	+10	−24	−52	
4	0	−20	−100	0
5	−31	−47	−73	+21
6	−16	−38	−65	−17
7	−20	−46	−86	
8	−50	−46	−93	−26
9	−21	−26	−33	−21
10	−20	−66	−73	−33

to 50 per cent decrease in the flow of bile below normal and a 13 to 69 per cent decrease in the flow of urine below normal in 10 nembutalized dogs (Tables III and IV).

Inhalation of mixtures of 10 and 5 per cent oxygen with nitrogen caused a further decrease in the flow of bile and urine. Acholia developed in 2 dogs and anuria was noted in 5 dogs.

The inhalation of 100 per cent oxygen for 30 to 45 minutes after the anoxemia resulted in an increase in the flow of bile and urine above that which was observed during the anoxemia;

TABLE IV.—EFFECT OF INHALATION OF VARIOUS OXYGEN CONCENTRATIONS UPON THE FLOW OF URINE IN THE NEMBUTALIZED DOG

Dog	Per cent oxygen inhaled for one-half hour			
	15 Per cent	10 Per cent	5 Per cent	100 Per cent
1	−45	−80	−87	−20
2	−64	−72	−100	−61
3	−69	−71	−89	
4	−52	−70	−63	−19
5	−56	−74	−87	−68
6	−33	−16	−100	− 8
7	−66	−75	−100	
8	−13	−73	−100	+5
9	−38	−57	−69	−42
10	−30	−100	−100	+33

in 3 dogs the flow was increased above the normal control level.

SUMMARY

The results of our investigations so far indicate that there is a physiological basis for the combined failure of liver and kidney function in some cases of intestinal obstruction. Liver function is first impaired by a nerve reflex inhibition due to distention of the intestine.

The anoxemia present in cases of severe intestinal distention, hyperthyroidism, and burns may produce a marked decrease in the formation of bile and urine. If mild, this may be a predisposing cause making the liver and kidneys more susceptible to other injurious agents. In some instances in which the anoxemia is severe, it may be the primary factor responsible for the combined failure of liver and kidney function and in some instances may produce an acholia and anuria.

Inhalations of high concentrations of oxygen are indicated when anoxemia is suspected as a factor in cases of impaired liver and kidney function.

PRINCIPLES OF PLASTIC SURGERY IN THE TREATMENT OF MALIGNANT TUMORS OF THE FACE

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MALIGNANT tumors of the skin occur most frequently on the exposed areas of the body, especially on the face; therefore, the appearance of the lesion or the increase in the size of a long standing cutaneous growth is recognized by the patient early in the course of the disease. However, the pathway open to him is an uncertain one, since there is conflict of professional opinion as to the ideal method of treatment for malignant lesions of the skin. Fear of facial disfigurement as a result of treatment is uppermost in the mind of the patient. Undoubtedly it is due to these factors that a high percentage of malignancies of the face are recurrent lesions when they are presented for surgical excision. In the management of the slowly growing, nonmetastasizing basal cell carcinoma of the skin, as well as in the more rapidly developing and metastasizing epidermoid carcinoma, the responsibility of the profession is great, for the vast majority of these lesions are curable if treated by an adequate method early in the course of the disease. If allowed to invade the bony structures of the face and head, they may be the cause of death. Therefore, it must be clear that the cardinal principle of any treatment which may be employed with safety is the complete destruction of the lesion. The general practitioner, in his advice to the patient with an early malignant tumor, must select one of four methods of therapy: electrodesiccation, x-ray therapy, radium therapy, or primary surgical extirpation. Reports in the literature concerning recurrent carcinoma of the skin indicate that the percentage of recurrence following electrodesiccation is sufficiently high to justify condemnation of this treatment. Although x-ray treatment is an efficient method of dealing with basal cell carcinomas, especially since it does not entail hospitalization and leaves minimal disfigurement, it has the disadvantages that therapy must be planned upon information obtained from biopsy and the entire growth is not available for microscopic study. Also the scarring of soft tissues produced by the ray may make it difficult to recognize a recurrence. Radium therapy has many of the same advantages and disadvantages as has x-ray therapy. The deforming scar which follows radium therapy often necessitates subsequent plastic excision. Surgery alone offers the satisfaction of complete extirpation of the malignant lesion and, in addition, the specimen is available for microscopic determination of the extent of its invasion. The single objection to surgery is the problem presented in the satisfactory restoration of the contour of the face—the appearance of the patient. If the removal of a malignant tumor of the face results in serious disfigurement, the patient is confronted with new difficulties, both economic and psychic, such as the loss of his job, or the development of an inferiority complex due to self-consciousness of his deformity. It is the object of this presentation to point out that, with a knowledge of the principles of plastic surgery, malignant tumors of the face can be treated successfully by surgery when first diagnosed and that the final cosmetic result is equal to or better than that of any other method. There is the additional satisfaction of knowing that the lesion has been removed completely. Once the lesion recurs following adequate primary irradiation, radical surgical extirpation certainly is justified. In this presentation certain principles of plastic surgery will be emphasized which come into play in the treatment of malignant lesions of the face and the subsequent restoration of appearance and function. If utilized by surgeons, they serve to place a high percentage

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of carcinomas of the face in the group which can be treated satisfactorily by surgery. If carcinoma of the face is to be dealt with by the surgeon, he should be familiar with and adhere to the following principles:

1. Generous estimate, in advance, of the tissue which must be removed with the lesion.
2. Consideration of Langer's lines of elasticity of the skin in planning the incision.
3. Use of the "temporary Thiersch graft."
4. Indications for the use of free grafts of skin, derma, fat, fascia, cartilage, and bone.
5. Use of pedunculated flaps.
6. Indications for the use of prostheses.

STATISTICS

From September, 1932, to September, 1940, exactly 100 patients were treated by surgery at the New York Hospital for malignancy of the skin of the face and neck. A histological classification of these tumors of the skin of the face and neck is presented in Table I.

TABLE I.—HISTOLOGICAL CLASSIFICATION

	Cases
Basal cell carcinoma	40
Recurrent basal cell carcinoma	14
Recurrent basal cell carcinoma invading bone	1
Epidermoid carcinoma	12
Recurrent epidermoid carcinoma	7
Epidermoid carcinoma invading bone	1
Recurrent epidermoid carcinoma invading bone	2
Epidermoid carcinoma of lip	10
Melanosarcoma	4
Sweat gland carcinoma	3
Epithelioma adenoides cysticum	1
Fibrosarcoma	1
Fibrosarcoma invading bone	2
Metastatic carcinoma from thyroid	1
Adamantinoma invading skin	1

Basal cell carcinoma. It should be stated here that it is not a fixed policy to treat all basal cell carcinomas of the skin by surgical excision. X-ray therapy is an efficient method of dealing with these growths and may be carried out without the expense of hospitalization. Thus, no time is lost from work and the therapy is effective with minimal facial disfigurement. However, it is interesting to note in a study of the 40 cases of basal cell carcinoma that primary surgical excision in tumors of the skin is as effective as x-ray and that the cosmetic results compare favorably with any other method. The follow-up on these cases shows that out of 40 there was only 1 which recurred following primary surgical excision. Thirty-nine cases are free from disease 3.1 years after operation: the rate of survival for 3 years without disease, therefore, is 94.7 per cent; the 5 year disease free survival rate is 90 per cent. The method of surgical treatment employed in these cases was as follows: simple excision, 20 cases; excision and thick split graft, 9 cases; excision and whole thickness graft, 11 cases. The anatomical distribution of the lesions in these 40 cases was as follows: on the nose, 11 cases; cheek, 9; neck, 5; eyelid, 5; chin, 3; ear, 3; temple, 1; forehead, 2; lip, 1.

Epidermoid carcinoma. Because of the high degree of malignancy of the epidermoid carcinomas and their tendency to metastasize, surgery is advised for them as a primary method of treatment. In the period of time covered by this survey, 12 cases of epidermoid carcinoma of the skin of the face and neck were treated by primary surgical excision. Anatomically these were distributed as follows: 3 cases of the ear; 3 of the nose; 2 of the cheek; 3 of the temple; 1 of the eyelids. The methods of surgical treatment were as follows: simple excision in 8 cases, excision and whole thickness graft in 1, excision and thick split graft in 2, excision and sliding flap in 1 case.

Metastatic cervical glands have been removed by block dissection or treated by x-ray therapy. Three of these patients were operated upon sufficiently long ago to be reported as 3 year cures. The follow-up at the present time shows that with the exception of 1 patient who died of heart disease 1 year after operation, all are free from disease at an average time of 1½ years after operation.

Recurrent basal cell carcinoma. In this interesting group there are 15 cases including 1 in which the recurrent growth had invaded the frontal bone. The previous treatment received by these patients is listed as follows:

	Cases
X-ray therapy, adequate dosage	4
X-ray therapy, amount unknown	1
Radium therapy, amount unknown	3
Desiccation	1
Electric needle	2
Surgical excision	1
Cauterization	1
Method of therapy unknown	2

TABLE II.—MALIGNANCY OF THE FACE INVOLVING THE BONE

Case	Lesion	Operative treatment	Result
1	Sarcoma invading maxilla	Resection of maxilla; temporal flap	Well after 3 years
2	Squamous cell carcinoma invading maxilla	Resection of maxilla; temporal flap	Well after 4 years
3	Recurrent basal cell carcinoma invading frontal bone	Resection of frontal bone and upper eyelid; scalp flap	Well after 8 years
4	Recurrent fibrosarcoma invading mastoid bone	Excision of tumor and external ear; cautery of bone; prosthesis	Well after 2 years
5	Recurrent adamantinoma of mandible invading skin	Resection of mandible with parotid gland and sacrifice of facial nerve; prosthesis	Well after 1 year
6	Recurrent epidermoid carcinoma invading orbit and temporal bone	Extirpation of orbit; resection of orbital bones	Died 8 months after operation of direct extension of lesion to brain and distant metastases
7	Recurrent epidermoid carcinoma invading skull	Resection of portion of parietal and frontal bones over sagittal sinus; thick split graft	Died 5 days after operation of meningitis and septicemia

The anatomical distribution of the lesions in these cases was as follows: 5 of the nose, 4 of the cheek, 3 of the eyelid, 1 of the temple, 1 of the forehead, 1 of the neck. The surgical treatment in the management of these recurrent lesions was as follows: excision, 2 cases; excision and thick split graft, 6; excision and whole thickness graft, 3; excision and sliding flap, 3; excision, sliding flap, and resection of frontal bone, 1 case. In all but 1 of these 15 recurrent tumors the primary treatment was other than surgery and in 12, or 80 per cent, the secondary radical excision gave a good clinical result. One tumor recurred 1 year after and another 6 years after radical surgical excision. A third patient could not be followed. Of the remaining 12 patients all are free from disease for periods varying from 1 to 8 years. Eight patients were operated upon sufficiently long ago to be reported as 3 year cures, 2 as 5 year cures; the percentage of 3 year cures, then, is 90, of 5 year cures, 66. These figures serve to emphasize the seriousness of recurrent basal cell carcinoma of the face. It is unfortunate that the primary treatment of these relatively benign lesions of the skin is inadequate so often. The most likely explanation of the situation is that simple methods of therapy afford cures in a high percentage of cases; the potential danger of these early lesions is not sufficiently emphasized; and there is a tendency on the part of both physicians and surgeons to be hesitant in recommending surgery in facial tumors because of the fear of disfigurement from postoperative scars.

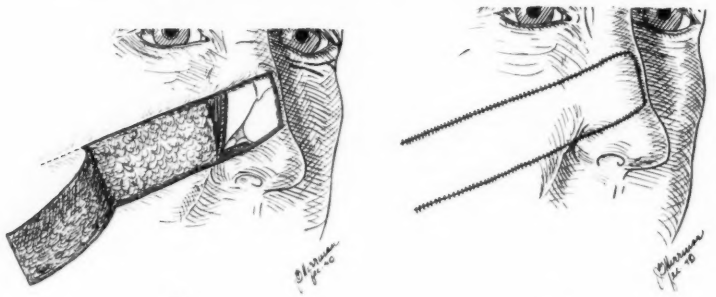
Recurrent epidermoid carcinoma. This group includes 9 cases, in 2 of which the recurrent lesion had invaded the underlying bone. The primary treatment in these cases was as follows:

	Cases
X-ray therapy, adequate dosage	2
X-ray therapy, amount unknown	3
Cauterization	2
Desiccation	1
Radium therapy	1

The anatomical distribution of the lesions was as follows: 3 cases of the neck, 3 of the eyelids, 1 of the forehead, 2 of the scalp. Extensive surgical resection was necessary in all of these cases and the surgical treatment comprised: excision in 3 cases; excision and whole thickness graft in 2; excision and thick split graft in 1; excision and prosthesis in 1; excision, resection of skull, and thick split graft in 1; excision, resection of orbital bone, thick split graft in 1. Seven of these patients (78 per cent) survived operation and have been free from disease for a period of time varying from 1 to 7 years. One patient died 1 year after extirpation of the orbit and removal of a portion of the temporal and orbital bones. There was 1 postoperative death following excision of a portion of the skull for infected carcinoma of the scalp. The fact that this was a case in which it was necessary to carry out extensive resection of bone calls attention to the increased danger of radical excision when the growth has invaded bone.

There were 7 cases in which the lesion of the face had involved the bone. These are listed in Table II.

1a 1d

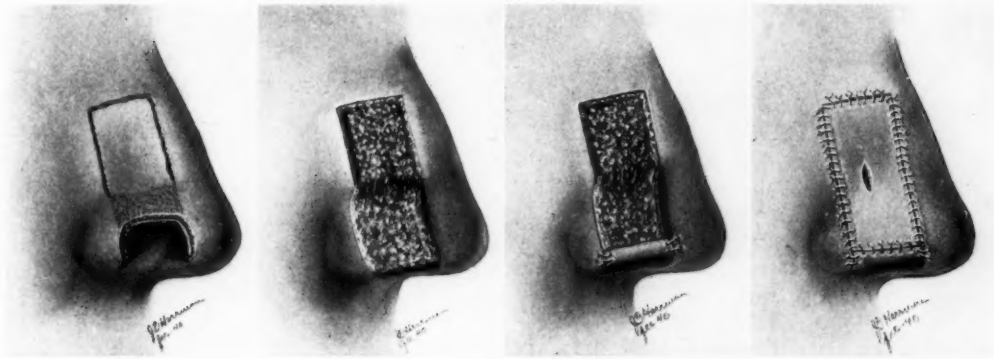


1b 1c

Fig. 1. Case 1. a, Basal cell carcinoma of the nose, twice recurrent. Excision and primary closure was done by means of a sliding flap from the cheek as shown in b and c. d, The appearance 9 months after operation. Follow-up examination 3 years and 4 months later showed no recurrence.

2a 2b 2c

Fig. 2. Case 2. a, Basal cell carcinoma of the nose. The lesion had recurred once following cauterization and twice following courses of x-ray therapy which were presumed to be adequate. b, Shows the extent of the whole thickness graft needed for replacement. Graft was taken from the cervical region. c, The appearance of the nose 2 months after operation was performed. No recurrence had occurred 4 years later.



b c d e

a f

Fig. 3. Case 3. a, Tumor of the skin and cartilage of the nose in a 32 year old man; the tumor proved to be metastatic from carcinoma of the thyroid. b, c, d, e, Show the steps involved in primary reconstruction of the nose after through-and-through resection of the skin, alar cartilage, and mucous membrane. b, The outline of a flap of skin from the upper portion of the nose. The epithelium was excised from the region inferior to the flap as indicated by the dotted area. c, The flap is swung downward to line the nose. d, The distal end of the flap of skin has been turned back on itself to provide a smooth cutaneous margin for the nostril. e, A whole thickness graft sutured in place over the raw area. f, The postoperative result. Examination 1 year after operation showed no recurrence in the nasal region though the patient is still receiving x-ray therapy to the cervical and thoracic regions.

The first and third cases in the above list will be referred to later in this report as Cases 5 and 4, respectively. The 2 deaths listed above have been recorded previously in the discussion of recurrent epidermoid carcinoma.

CASE REPORTS

Case 1 illustrates the use of sliding flaps from the neighborhood to cover the defect of soft tissue after excision of malignant tumor.

Case 1. A. W., New York Hospital No. 208378, a 57 year old woman, presented herself for treatment of an infiltrating lesion of the right side of the nose which was noticed for the first time 10 years before admission and which had recurred following 2 surgical excisions performed in another institution 9 and 5 years ago. Rectangular excision of this recurrent basal cell carcinoma was done and the defect was closed by means of a sliding flap of skin and subcutaneous tissue as shown in Figure 1. No recurrence 3½ years later.

Free grafts of skin which are available for the repair of defects created by surgical excision of malignant tumors of the skin of the face include the following: (1) the Ollier-Thiersch graft or razor graft (3); (2) the thick split graft (1); (3) the three-quarter thickness or intermediate graft (5); and (4) the whole thickness graft (2). The chief value of the Ollier-Thiersch graft lies in the fact that its epithelial surface affords cutaneous healing of the wound after excision of a growth and scar formation is prevented. However, the appearance of the grafted area is unsatisfactory. Therefore, the use of such grafts on the face as a final measure is condemned. As a temporary method this thin graft allows for observation of the operation site for recurrence of the tumor and affords time for the preparation of a suitable flap of soft tissue. The term "temporary Thiersch graft" has been coined to describe this graft; the material available for it is nearly inexhaustible for it is readily obtained from the thigh or torso. The thick split graft and the intermediate graft are

a e

b c d

Fig. 4. Case 4. a, Basal cell carcinoma which had recurred 5 times and had invaded the frontal bone and upper eyelid. b, Outline of radical excision. c, Diagram of defect after excision of tumor, skin, frontal bone, and upper eyelid in one block had been made. d, Technique of forward rotation of scalp flap. Parietal region of skull and upper eyelid were surfaced with thick split grafts. e, Postoperative appearance of patient. No recurrence of carcinoma 8 years after operation. Patient refused further reparative surgery.

thicker than the Thiersch; the intermediate embodying 75 to 90 per cent of the thickness of the skin. Although some plastic surgeons use the intermediate graft for facial reconstruction because of its ready availability, the whole thickness graft is preferred at the New York Hospital because of the superior cosmetic result achieved by its use. The whole thickness graft, as implied by its name, embodies all of the layers of the skin and is cut according to pattern of the defect. The use of this graft leaves little to be desired since it provides an accurate match to the adjacent skin of the face in color, texture, moisture, and movability on the underlying tissues. The upper eyelid, from which a graft 3 by 1.5

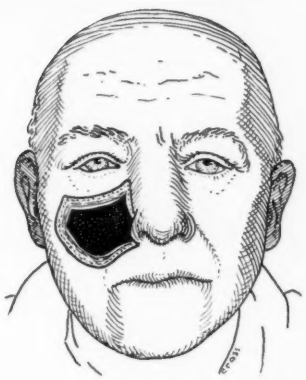
a c d

Fig. 5. Case 5. a, Fibrosarcoma of cheek invading the maxilla. b, Diagrammatic representation of the defect after radical excision of tumor together with anterior wall of maxillary sinus and hard palate. c, Tubed temporal flap sutured into the maxillary defect. The medial portion of this flap had been converted into a double faced flap by burying a thick split graft under it at an earlier operation. d, Appearance after division of the pedicle and resuture of its base into the temporal region. No recurrence 3 years and 2 months later.

centimeters in size can be cut without producing deformity, and the postauricular area, which may yield a graft of 5 by 3.5 centimeters, are ideal sources for such grafts. If a large graft is required a donor area on the abdomen is necessary but it must be selected with due consideration for the growth of hair.

Case 2 demonstrates the successful result obtained with the use of a free, whole thickness skin graft to surface the defect produced by the excision of a malignant tumor of the skin.

Case 2. V. L., New York Hospital No. 60215, a 50 year old woman, was presented for treatment of a basal cell carcinoma of the skin of the right side of the nose which was three times recurrent following x-ray therapy. At operation on September 29, 1937, this recurrent basal cell carcinoma was removed by excision as shown in Figure 2. All soft tissues were removed down to the bone and cartilage. A patterned whole thickness graft, which was cut from the posterior triangle of the neck, was sutured into the defect. Follow-up examination 4 years after operation showed no recurrence.



b

Case 3 demonstrates the method of rotation of a skin flap to provide a lining of skin in the repair of a through-and-through defect of the soft parts of the nose. The danger of relying entirely on biopsy material for a final tumor diagnosis is dramatically emphasized.

Case 3. J. K., New York Hospital No. 94807, a 32 year old man, was subjected in 1935 to subtotal thyroidectomy. Microscopic examination of sections cut from the specimen showed this to be a papillary adenocarcinoma of the thyroid. Intensive radiation was given to the neck and chest. Apparently the disease was under arrest when in February 1940 he noticed the development of a nodule over the alar cartilage of the nose on the right side. X-ray therapy

a b c

Fig. 6. Case 6. a, Recurrent epidermoid carcinoma of eyelids with extension to the globe. b, Deformity after enucleation with sacrifice of both eyelids; the cavity has been surfaced by application of a thick split graft. c, Appearance of patient after fitting with a glass eye attached to latex prosthesis. No recurrence 2 years and 4 months after operation.

failed to retard the growth of this lesion. The biopsy report was "spiroadenoma" or benign sweat gland adenoma. Because the appearance of the lesion suggested the invasive tendency of this tumor, radical excision was done on September 28, 1940. The entire thickness of the wall of the nose including skin, cartilage, and mucous membrane was removed as shown in Figure 3. The technical problem in this case was to provide a method of repair which afforded skin to line the nasal cavity and also to surface the wound. This could have been done by the use of a double faced flap from the cheek had such a flap been prepared earlier. The technique of rotation of a flap downward from the upper portion of the nose to form a lining and of surfacing the area with a whole thickness graft taken from the retroauricular area is demonstrated in Figure 3. With the entire tumor at his disposal for examination the pathologist was able to ascertain that it was a metastatic carcinoma of the thyroid. The graft healed nicely with good cosmetic effect. Multiple pulmonary metastases developed subsequently. At the present time the patient is still receiving x-ray treatments to the lung fields.

Cases 4, 5, and 6 are examples of the surgical management of advanced malignancy affecting the eye and the bones of the face. Radical surgical excision in cases of this type calls for boldness and courage since excision of any of the facial bones produces deformity which in itself may constitute cause for complete disability. It is in the management of these patients that a knowledge of reparative techniques and of the applications of prostheses offers the prospect of cure with rehabilitation. Although in theory, prostheses represent the final failure of plastic surgery, their use has served to rehabilitate many unfortunate individuals and to contribute greatly to their happiness.

Case 4. D. W., New York Hospital No. 41493, a 51 year old man, in 1933 presented himself for treatment of a basal cell carcinoma of the forehead invading the frontal bone. Over a period of 14 years this lesion had recurred 5 times following x-ray and radium therapy. Examination at the New York Hospital in 1933 disclosed the ulcerated lesion of the right forehead as shown in Figure 4. The growth had invaded the frontal bone, had destroyed the eyebrow, had produced some weakness of the superior rectus muscle. Vision in both eyes was good. There was extensive scar above the ulcerated area. Excision of the tumor in this case was done by Dr. George Heuer. The entire mass including the skin, the muscles of the upper eyelid, the frontal bone, and some of the fatty areolar tissue of the orbit was removed in one block. The frontal sinus was opened in the course of the resection. The dura mater appeared normal. Closure of the defect in the forehead was accomplished by the forward rotation of a flap hinged at the median sagittal line of the scalp. A thick split graft taken from the right thigh was used to cover the raw area on the parietal region of the skull produced by the forward rotation of the flap. A second smaller thick split graft was used to surface the right eyelid. The growth of hair in the right forehead region was arrested by means of x-ray treatment. The patient has now survived 8 years since

operation was performed. There is no local recurrence and he is in excellent general health. The appearance of the concave frontal area and the ptosis of the right eyelid have not bothered the patient sufficiently to convince him that it would be worth while to undergo further operation for cosmetic improvement.

Case 5. E. W., New York Hospital No. 192441, a 59 year old man, was examined at the New York Hospital for the first time in January 1938 because of a swelling of the right cheek and obstruction of the nasal passages on the right. Antiluetic and x-ray therapy had been administered without change in the size of the lesion. Examination showed a firm mass measuring 6 by 6 centimeters over the right maxilla. The mass was adherent to the skin and to the underlying maxilla. The nose was partially distorted as shown in Figure 5. Biopsy showed that the tumor was a retothelial (reticulocell) tumor of the face involving skin, subcutaneous tissue, and bone. On August 30, 1938, radical resection of the maxilla was done by Dr. William F. MacFee according to the technique described elsewhere by him. It was possible to save the bony floor of the orbit, the posterior wall of the maxillary sinus, the soft palate and the right upper lip. The hard palate was removed. Mucous membrane was sutured to skin wherever possible. The patient made an uneventful recovery. On March 16, 1940, approximately 7 months after resection of the maxilla a temporal flap was fashioned at operation and sutured down in place as shown in Figure 5. Division of the flap at its medial end was done on March 25, 1940. On April 10, 1940 the flap was re-elevated and two thick split grafts were taken from the thigh and buried face to face under the upper and medial end of the flap. This served to make the flap a double faced one in its distal portion. When the flap was elevated again at operation on May 6, 1940 the donor area over the frontal bone was found to be neatly surfaced by the thick split graft which had been placed at the previous operation. The pedicle was tubed by suture and its distal, double faced end was transplanted to the maxillary region as shown in Figure 5. In the final operative procedure the pedicle was detached and its base was replaced in its normal position in the preauricular and temporal regions. The patient has been equipped by Dr. Harold Genvert of this clinic with a nicely fitted upper dental plate which carries an obturator to fit into and fill the defect in the hard palate. Follow-up examination 3 years and 2 months after excision of the tumor showed the patient to be in excellent general condition with no evidence of recurrence or metastasis.

Case 6. I. M., New York Hospital No. 237954, a 64 year old woman, had a tumor of the lower eyelid removed by her physician by cautery in 1936 and again in 1938. Examination in July, 1939, showed an adherent ulcerated tumor of the skin near the inner canthus of the right eyelid. The tumor involved nearly half of the upper and lower lids. There was congestion of the conjunctiva and the tumor could be seen growing out onto the cornea. There was dimness of vision but not complete loss of sight. There was no cervical adenopathy. Enucleation was necessary to effect cure. The appearance of the lesion is shown in Figure 6. At operation on July 19, 1939 the eyeball together with both eyelids and all orbital structures was removed. Microscopy showed the tumor to be an epidermoid carcinoma. A thick split graft was applied to the wound after wrapping it about a mass of dental stent, previously molded to fit the cavity. The orbital bones were exposed in the floor of and on the medial aspects of the wound. It was not possible to preserve enough of the lower eyelid to help in the application of a prosthesis. The patient was fitted with a glass eye which is held in the socket by means of a latex prosthesis (6). This patient reports every 3 months for inspection of the grafted area. At these visits the prosthesis is retinted, replaced and held by means of liquid adhesive. There has been no recurrence to the present date, 2 years and 4 months after operation.

SUMMARY AND CONCLUSIONS

In this report an analysis is made of 100 cases of malignancy of the face treated by surgery over an 8 year period. There were 55 cases of basal cell carcinoma of which 15, or 27 per cent, were recurrent tumors when presented for surgical treatment. There were 21 cases of epidermoid carcinoma of which 9, or 43 per cent, were recurrent tumors. Study of these records shows that in the majority of the recurrent tumors, primary treatment had been inadequate. This analysis of data serves to emphasize the responsibility of the doctor to provide adequate curative primary treatment for malignant lesions of the face. In 7 cases of the 100 in the series, the tumor had invaded the bones of the face. The indications for the use of grafts, flaps, and prostheses are demonstrated by means of 6 detailed case reports. If utilized by surgeons, the principles of reparative surgery serve to assign a high percentage of malignant tumors of the face to treatment by radical surgical excision.

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THE USE OF VERMILION BORDERED FLAPS IN SURGERY ABOUT THE MOUTH

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VERMILION bordered flaps have proved one of the most effective methods of correcting defects or deformities about the mouth. Although American authors commonly attribute the operation to Abbe, the method was first described by Estlander in 1872, 26 years before Abbe's paper appeared.

Estlander's paper was published in Swedish in the *Nordiskt medicinskt Archiv* under the title "A Method of Replacing Lost Tissue in one Lip and Cheek from the Other Lip." A similar report from him appeared that same year in the *Archiv fur klinische Chirurgie* (6). A later description of his method was published in French in 1877 (7); it is much the same as that of the original paper.

Estlander had observed that after wide excision of the lower lip for malignant disease, closure was possible only with tension on the skin margins and a great difference in the width of the lips. He decried the tendency among surgeons, when confronted with a large defect in the lip, to search out and utilize remote tissues from the cheeks or neck, "neglecting entirely the most available tissue—namely the other lip." While studying the anatomical relationships of the vessels about the mouth he realized that large flaps could be nourished by the encircling coronary artery alone. He determined and described accurately the relation of this vessel to the skin and mucosa of the lip and indicated the importance of this relation in avoiding injury to the vessel while preparing the flap and turning it on its narrow pedicle. Several case histories and complete descriptions of the operations are presented to indicate where and how the procedure is applicable. There are illustrative drawings of one of these cases showing how, by use of this method, the defect from excision of half of the lower lip for carcinoma was repaired by switching a flap from the upper lip. A new corner of the mouth was formed by the pedicle. In another case there was loss of one ala of the nose, part of the upper lip, and the adjacent cheek as a result of a noma. Estlander illustrates its correction with a large, vermilion bordered flap turned up from the lower lip. One margin of the flap was cut across and adjusted to form

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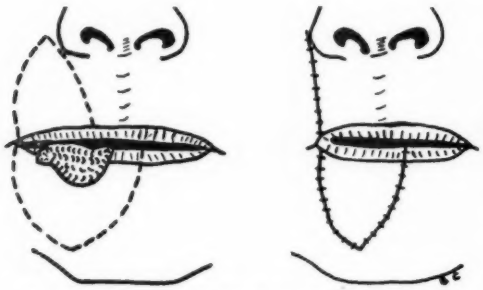

Fig. 1. Illustrating the use of a vermilion bordered flap in the primary repair of a defect from a wide excision of the lower lip, adjacent to the corner of the mouth. a, Left, dotted lines indicate the area excised from lower lip and outline of flap of the upper. b, The completed repair.

Fig. 2. A patient in whom excision and repair were carried out by method which is illustrated in Figure 1. The narrow pedicle, on which the flap is carried, can be seen.

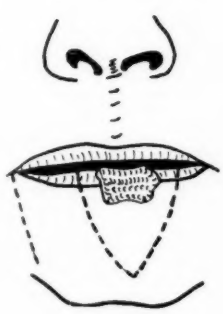

Fig. 3a.

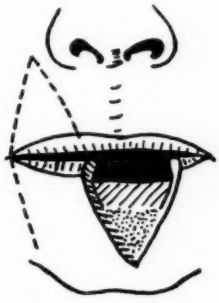

Fig. 3b.

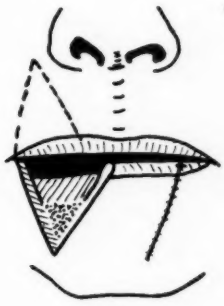

Fig. 3c.

Fig. 3d.

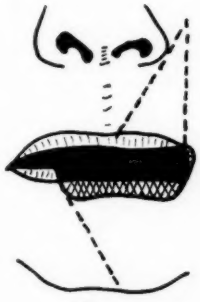

Fig. 5a.

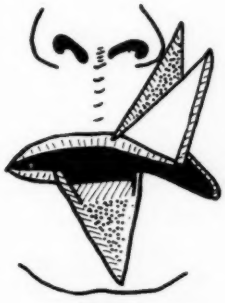

Fig. 5b.

Fig. 5c.

Fig. 4.

Fig. 6.

Fig. 3. Illustrating the use of a vermilion bordered flap in the primary repair of a defect from a wide excision of the center of the lower lip. A quadrangular flap is shifted into the midline defect and the repair is completed by the flap from the upper lip. a and b, The dotted lines indicate the area excised from the lower lip and the outline of the quadrangular and triangular flaps; c and d, the shifting of the flap and the completed repair.

Fig. 4. A patient in whom excision and repair were carried out by method shown in Figure 3.

Fig. 5. Illustrating the use of a vermilion bordered flap in the repair of a pre-existing defect in the lower lip. a, The defect is outlined and the incisions are indicated by means of dotted lines. In b, the shifting of a local triangular flap in the lower lip and a vermilion bordered flap from the upper is illustrated. In diagram c, the completed repair is shown.

Fig. 6. A patient in whom surgical repair was carried out by method which is shown in the diagrams of Figure 5.

the ala, the remainder fitted to the lip and cheek. In this case also a corner of the mouth was formed by the pedicle.

Abbe's paper in 1898 was the first description of the operation in English, and the first in which the pedicle crossed the mouth and was later severed. He reported a single case and only briefly outlined and illustrated the method. His contribution should be considered a modification of the original method

Fig. 7a.

Fig. 7b.

Fig. 7c.

Fig. 8.

Fig. 7. Illustrating the use of a vermilion bordered flap in secondary correction of a unilateral harelip deformity. a, Showing the tight retracted upper lip and deficient floor of the nose. The outline of the flap is indicated by dotted lines. b, The flap is in place in the upper lip with the pedicle crossing the mouth. c, The completed repair showing relaxation of the upper lip and correction of the floor of the nose.

Fig. 8. A patient in whom secondary correction was carried out by method shown in Figure 7.

and full credit is due Estlander for the introduction of its fundamental concept many years before.

The indications for the use of vermilion bordered lip flaps have been demonstrated and extended by surgeons in recent years (2, 3, 8, 9), and there have been modifications of the flap itself (4) but the primary principle, which consists of carrying a large, direct vermilion bordered flap on a narrow pedicle with a single nutrient artery has remained unchanged.

The simplest use of the flap is one in which there is a defect in the lower lip, adjacent to the corner of the mouth, too large for primary closure. This method is similar to that used by Estlander in one of his illustrative cases (Figs. 1 and 2).

CASE 1. C. P. H. 40–731. A man, 57 years of age, had a large, irregular, ulcerated lesion of the right lower lip 1.5 centimeters in diameter which extended deeply into the substance of the lip and which proved to be squamous cell carcinoma, grade II. The operation was done under a local anesthetic. The two mental nerves, the right infraorbital, and the few cervical branches that reached upward to the chin were blocked with 1 per cent novocain. Nerve block is preferable to local infiltration because infiltration may jeopardize the blood supply to the flap by local trauma and tension within the tissues. A wide V-excision of the diseased area was then carried out. This involved removal of over half the lower lip, from the corner of the mouth to beyond the midline on the opposite side and down to the alveolus. A large triangular flap, half the width of the defect, was then raised from the upper lip and cheek in the nasolabial fold and turned downward into its new position. The pedicle of the flap containing the coronary artery formed a new corner of the mouth. It was carefully sutured in place, with

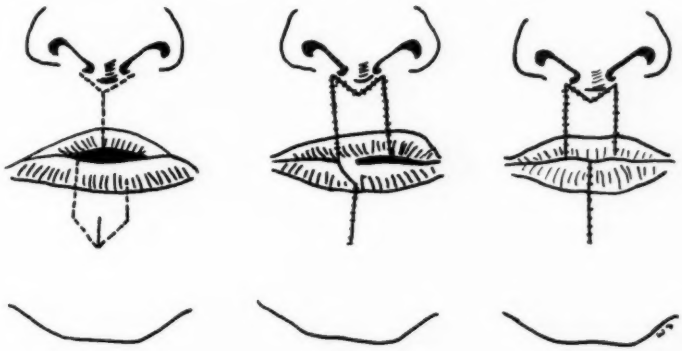

Fig. 9a. Fig. 9b. Fig. 9c.

Fig. 10.

Fig. 9. Illustrating the use of a split vermilion bordered flap in the secondary correction of a double harelip deformity. a, The dotted lines indicate the outlines of the flap and the incision in the upper lip. b, The flap is in place in the upper lip with the pedicle crossing the mouth. c, The completed repair.

Fig. 10. A patient in whom the prolabium was excised and replaced with a split vermilion bordered flap.

deep vertical mattress sutures in the mouth and fine interrupted silk sutures in the skin. A right suprahyoid dissection was done 6 months later because of a palpable node but no metastases were found. There has been no recurrence after a full year.

This patient, before operation, was fearful that extensive relaxing incisions would be necessary in the cheek and that he might lose his job because of his appearance. The functional and cosmetic results, however, by this method, are very satisfactory to the patient.

A second method is used when the neoplasm involves the center of the lower lip. If the defect is so large that it cannot be closed primarily, a quadrangular flap extending to the corner of the mouth is shifted into the defect and the repair is completed in a similar manner to that of the first method (Figs. 3 and 4).

Case 2. C. P. H. 22–1144. A man 56 years of age, had a large, round, ulcerated lesion of the middle of the lower lip 2 centimeters in diameter which proved to be squamous cell carcinoma, grade I. At operation, also with local nerve block anesthesia, a wide V excision of the diseased area was carried out. This involved the removal of over one-half the center of the lower lip. A quadrangular flap of normal lip was shifted across the midline to the left, and the remaining defect was closed with a triangular vermilion bordered flap turned down from the upper lip. Neck dissection has not been done but the patient is under careful observation.

A third method is useful when there is a pre-existing defect from surgical excision of the lip for carcinoma or for other causes. A triangular or rectangular flap from the upper lip is turned into the defect in the lower and the adjacent tissues adjusted to it (Figs. 5 and 6).

Case 3. P. M. H. 40–1003. A man, 76 years of age, had a squamous cell carcinoma, grade III of the lower lip with metastases to the neck. The excision of the lesion of the lip and a left radical neck dissection were done by Dr. C. C. Franseen. At operation,

8 months later, a triangular vermilion bordered flap was raised from the left upper lip. There was no hazard in using this flap because, although the left facial artery had been severed in doing the neck dissection, that on the right, which is the side from which the flap is nourished, was intact. By extending an incision obliquely downward from the right border of the defect in the lower lip a triangular space was created into which the flap was switched. The second flap, thus formed from the lower lip, was shifted to the newly created corner of the mouth on the left and adjusted to the adjacent cheek.

A fourth method, similar to that described by Abbe, is useful in the secondary correction of unilateral harelip deformities. The tight upper lip and the often deficient floor of the nose can be improved by utilizing a flap from the lower lip, giving a more pleasing relationship between the two. By this method both the fullness of the lower lip is reduced and tissue is added to the upper lip. The pedicle which must cross the mouth is severed after 2 to 3 weeks (Figs. 7 and 8).

CASE 4. M. G. H. 126,720. Patient is a girl, 15 years of age. The primary repair of the lip, done in childhood, left her with a tense retracted upper lip, a deficient floor of the nose, and unfortunately, with ugly suture marks on both cheeks. At operation, under intratracheal ether anesthesia, the difference in width between the two lips was determined and a vermilion bordered flap half this width was prepared in the midline of the lower lip. The old scar in the upper lip was opened and extended into the floor of the nose. The flap was turned into this defect; the vermilion borders were accurately approximated; and the tip of the flap was fitted into the floor of the nose. Two weeks later the pedicle of the flap was severed and the mucosal edges were closed. Most of the operative procedures were carried out by Dr. S. H. Sturgis.

A fifth method is useful for secondary corrections following harelip repair when there is nasal symmetry. The lip is opened in the midline with extensions across the base of the columella into the floor of each nostril. A split vermilion bordered flap is used. The splitting of the flap leaves a better balanced lip with scars that are not apparent (Figs. 9 and 10).

CASE 5. M. G. H. 259,127, patient of Dr. M. S. Strock. A girl, 13 years of age, had a partial double harelip repaired in childhood. In the initial repair the prolabium was utilized to form the vermilion border in the midline. Because of the notching of the upper lip and because of the deficiency of tissue bulk in the prolabium, a split vermilion bordered flap from the lower lip was used. At operation, under general anesthesia, instead of opening the lip in the midline, as indicated in the diagram, the prolabium was completely excised in this case and replaced by the flap.

When the pedicle of the flap forms a new corner of the mouth, as in the first 3 cases, it can later be severed just as is the pedicle that crosses the mouth. In this way the width of the opening is increased and the patient can use the mouth more comfortably. It is important, however, not to extend the incision laterally beyond the pedicle of the flap as the patient may then have difficulty in controlling the corner of the mouth and in preventing the leakage of saliva. After the patient has become accustomed to the altered condition of the mouth there is seldom much difficulty with function, for sufficient residual muscular action remains to control the motions of the mouth. The scars of the face and lips resulting from the procedures are not disfiguring because they lie in the nasolabial fold and vertically on the lip. Little distortion of the mouth is caused by the scars either at rest or while the mouth is in motion.

SUMMARY

The vermilion bordered lip flap was first described by Estlander in 1872. It is useful in repairing the lip after a wide excision for carcinoma, as the need of widespread relaxing incisions in the cheek is eliminated and no normal tissue is sacrificed. It is also useful for the secondary correction of harelip deformities both in securing a better balance between the upper and lower lips, and in replacing deficiencies in the floor of the nose. Five cases in which the flap was used are presented.

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HYPOPROTHROMBINEMIA AND LIVER FUNCTION

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PLASMA prothrombin and methods for measuring this clotting factor have attracted much interest in recent years. Even before the need for vitamin K was known, it had been shown (18, 22) that intact liver function is necessary for the production of prothrombin. With the widespread clinical use of vitamin K, it soon became apparent that liver disease interferes with the prothrombin response to vitamin K therapy in human patients (4, 5, 6, 13, 16, 19, 20). Additional studies with liver extirpation confirmed the vital rôle of the liver in prothrombin production (1, 20, 23). Hypoprothrombinemia, thus, may result either from a deficiency in vitamin K, or from liver disease. This necessity of a good state of liver function to maintain normal prothrombin production naturally has suggested the possible use of the prothrombin level as a measure of liver function. Wilson (24, 25) studied the correlation of the prothrombin level and the hippuric acid liver function test and concluded that these two usually gave parallel results and reflected the state of the liver much better than did other liver function tests. More recently Lord and Andrus (8) and Olwin (11) have stressed the value of the prothrombin level and the response to vitamin K in the differential diagnosis of intrahepatic and extrahepatic jaundice. On the other hand, Lucia and Aggeler (10) found little correlation between the hippuric acid liver function test and the prothrombin level. Lucia and Aggeler used the prothrombin method of Quick (14, 15) whereas the others used the two stage method of Warner, Brinkhous and Smith (18, 22). It appears probable that differences in the prothrombin methods employed are responsible for the differences in the results obtained by these workers.

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We wish to present studies correlating the plasma prothrombin level with other evidence of liver disease, and, particularly, to compare the results obtained with different prothrombin methods. The data obtained so far indicate that in human patients hypoprothrombinemia which does not respond to vitamin K therapy is a reliable index of liver disease and that prothrombin techniques differ in sensitivity in this respect.

Before presenting the cases studied, we wish to give a brief résumé of the prothrombin methods available. The several prothrombin methods in current use in this country fall into two groups and can be classified as one stage and two stage methods. In the two-stage procedure, developed by Warner, Brinkhous, and Smith (18, 22), the prothrombin of plasma is converted into active thrombin as a preliminary step. In a second step, the thrombin thus produced is measured by determining the speed with which it will clot a standard fibrinogen solution. In contrast, the one stage methods simply measure the clotting time of blood or plasma in the presence of excess thromboplastin. These latter methods, thus, are dependent upon a summation of the time required for the thrombin to act in clotting. They serve as a very practical index of the capacity of the blood to clot and, thus, of the tendency of the patient to bleed. The method of Quick (14, 15) and the more simple "bedside" test (27) developed in our laboratory, which gives essentially the same results as the Quick's method, are of this type. Also several modifications (3, 7, 26) of these are in this category.

All of the methods in current use give satisfactory results for the clinical control of vitamin K therapy, and all serve to detect the hypoprothrombinemia which results from acute severe liver injury. However, with milder degrees of hypoprothrombinemia, particularly if of a chronic nature, it appears that an altered convertibility of prothrombin

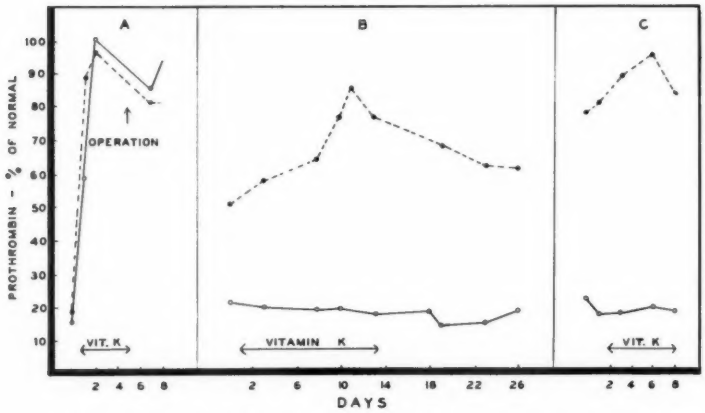

Fig. 1. Prothrombin response to vitamin K therapy. A, Stricture of bile duct; B, portal cirrhosis; C, Banti's disease. - - • - -, Bedside technique; —o—, two stage technique.

may compensate for a considerable decrease in the actual amount of prothrombin present (12, 28). In instances of this type, the two stage method appears to be a much more sensitive index of the true prothrombin level than are the one stage methods and, therefore, is a better index of liver function.

Figure 1, A, represents a case in which an obstruction of the common bile duct resulted in vitamin K deficiency. The hypoprothrombinemia, shown by both the two stage and the one stage methods, responded promptly and completely to the administration of the vitamin. In this case, by all available criteria, the functional capacity of the liver was within normal limits and the lowered prothrombin was due entirely to a vitamin K deficiency.[1] This case illustrates the normal response to vitamin K therapy.

Figure 1, B, represents a case of portal cirrhosis of the liver. Bile was present in the bowel, and there was no reason to suspect that the vitamin K intake was inadequate.

[1]We believe that for the purpose of ensuring a maximum response with the greatest speed, the best way to administer this vitamin is by the intravenous injection of one of the synthetic water soluble preparations.

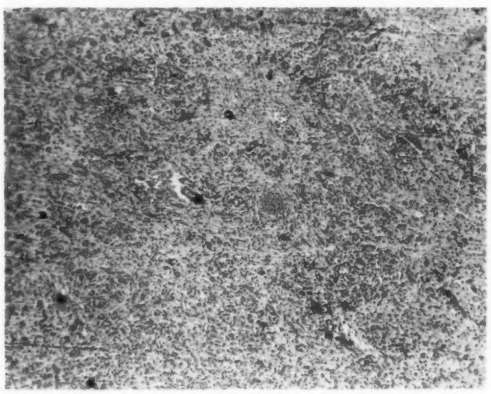

Fig. 2. Microscopic section of liver from case of extensive cirrhosis of liver which did not respond to vitamin K therapy.

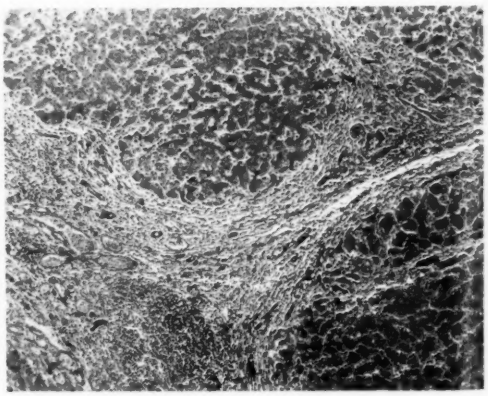

Fig. 3. Microscopic section of liver, showing extensive cirrhosis, from case of Banti's disease which did not respond to vitamin K therapy.

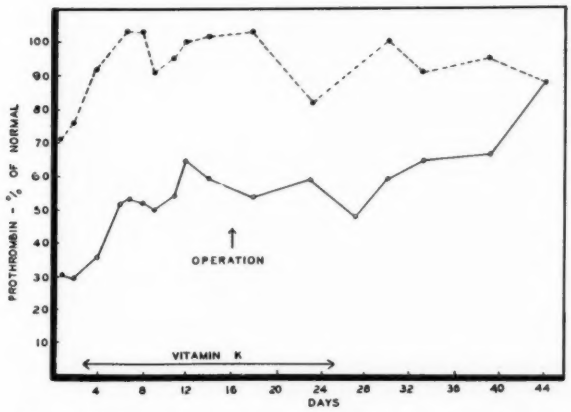

Fig. 4. Prothrombin response to vitamin K therapy. Central liver necrosis. - - •- -, Bedside technique; —o—, two stage technique.

The amount of prothrombin, as indicated by the two stage method, was greatly reduced. The clotting power of the blood, however, as indicated by the one stage method was only moderately impaired. As would be expected in cases in which the lowered prothrombin was due primarily to liver disease, vitamin K did not correct the hypoprothrombinemia. A poor and incomplete response was indicated by the one stage test, but no response was demonstrable by the two stage test. The patient came to autopsy, and an extreme degree of cirrhosis of the liver (Fig. 2) was found. This marked liver damage, indicated by the ineffectiveness of vitamin K, was mainly responsible for the hypoprothrombinemia.

Figure 1, C, represents a case of Banti's syndrome. Here again, the hypoprothrombinemia was associated with extensive liver damage and the administration of vitamin K was ineffective. As in the preceding case, the two stage prothrombin method proved to be a more sensitive index of the liver damage than did the one stage test. The hypoprothrombinemia, as indicated by the two stage method was much more severe than was apparent from the one stage test. Also, the ineffectiveness of vitamin K was more evident by the two stage method. We have noted that there is usually some shortening of the one stage clotting time following vitamin K therapy, irrespective of the type case with which we are dealing. The biological significance of this fact is not yet apparent. This patient died following splenectomy and the liver (Fig. 3) showed extensive cirrhosis.

Figure 4 represents a case of hepatitis with jaundice. In this case the prothrombin level showed some response to vitamin K by both methods, indicating, we feel, that there was some deficiency of this vitamin. The main cause for the lowered prothrombin, as well as of the jaundice, however, was the liver damage, and the more sensitive two stage prothrombin method indicated a very incomplete response. This patient was explored and the

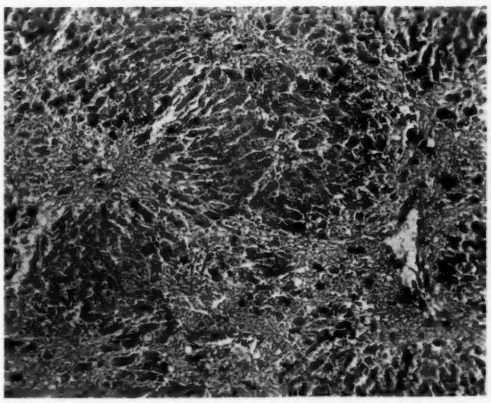

Fig. 5. Microscopic section of liver in case of severe hepatitis with jaundice.

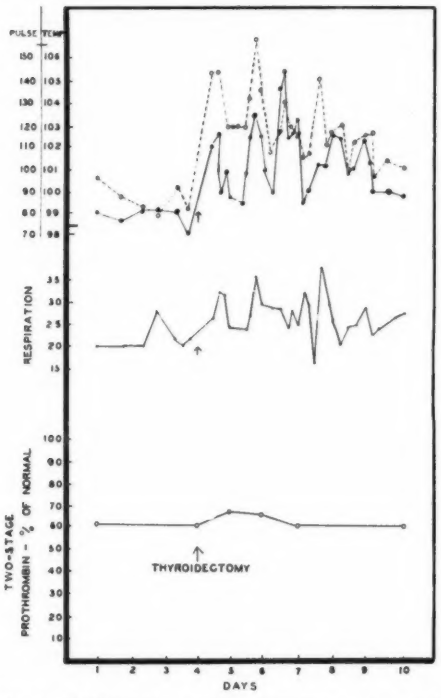

Fig. 6. Prothrombin level; temperature, —•—; pulse, --o--; and respiration in a case of thyroid crisis with recovery.

extrahepatic biliary tract was found to be entirely normal. The very gradual return of the prothrombin level to normal coincided with clinical recovery of the patient. A biopsy of the liver, at the time of exploration showed extensive liver necrosis (Fig. 5). This case is one in which the extensive liver damage, indicated by the two stage method, strongly suggested that the jaundice was of intrahepatic origin before exploration, and illustrates the usefulness of prothrombin studies in differential diagnosis as well as in prognosis.

During the past few years, increased emphasis has been placed on changes occurring in the liver associated with hyperthyroidism, (2, 9, 17). Figure 6 represents a case of thyroid crisis with recovery. The preoperative and postoperative prothrombin levels were moderately reduced indicating moderate impairment of liver function in this case. Still more striking is a recent fatal case of postoperative thyroid crisis. In this patient the prothrombin level, as determined by the two stage method, fell to 16 per cent of normal. Vitamin K therapy was instituted, but the patient died before a second prothrombin determination could be made. Extensive hemorrhage, no doubt due to the lowered prothrombin, was at least a contributing factor in the fatal outcome. These 2 cases, of course, are not sufficient to justify ultimate conclusions, but they are in accord with the thesis that hepatic insufficiency is an important factor in fatal thyroid crisis.

In all of the cases we have studied, the two stage procedure has appeared to be a more sensitive index of liver damage than have the one stage tests. If further work establishes prothrombin determinations as a useful index of liver function, it may be that some simplification of the two stage test can be developed which will render it more suitable for general use.

SUMMARY

From our results, as well as from reports in the literature, it appears that determination of the prothrombin level has considerable promise as an index of liver function. Hypoprothrombinemia due to a vitamin K deficiency responds rapidly to specific therapy. Failure to obtain this response appears to indicate liver disease.

Unfortunately, it appears from the work to date, that the simple one stage tests, which have proved so satisfactory for the control of vitamin K therapy, are not nearly as sensitive an index of liver damage as is the more complicated two stage method. The latter method could probably be simplified.

Preliminary studies of prothrombin levels in thyroid crisis lend some support to the thesis that the liver is concerned in this condition.

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THE HEALING OF ANASTOMOTIC WOUNDS IN ASEPTIC GASTRIC SURGERY

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THE object of this paper is to report some of the work done in the experimental laboratory during the development of a technique for aseptic gastric surgery. During the past 2 years all gastric operations on the surgical clinic service at the Stanford University Hospitals have been done with a closed or aseptic procedure. The technique of this operation and the clinical experiences with its use have been reported by Dr. Emile Holman. In the early stages of the conversion from open anastomosis to an aseptic technique certain questions arose relative to the use of clamps, methods of suturing, and the healing of wounds made with the cautery.

Although aseptic anastomosis in the intestine has been practiced for many years, the use of this principle in gastrointestinal surgery has found few advocates. Wangensteen (14) recently described a method of doing closed anastomoses adaptable to any segment of the alimentary canal, and followed this publication with another (15) in which he described his experiences with the technique after using it in 100 consecutive cases. As Wangensteen indicated, probably the following two factors, more than any others, have deterred surgeons from using a closed anastomosis; namely: danger from hemorrhage and fear of poor mucosal healing if the mucous membranes are not approximated.

Three choices are open to the surgeon in preventing bleeding in gastric surgery. The first is the clamping and ligating of the individual gastric vessels, which method is tedious and necessarily involves spilling some blood and gastric content into the operative field. The second is the use of a continuous hemostatic suture as an inner layer which must be placed tightly enough to constrict the vessels. Such constriction is injurious to the tissues. Healing with this type of suture has been found to be poor and is attended by considerable edema and infection (9). The third method is the use of the cautery to sear the wall sufficiently to coagulate the vessels.

Few studies have been reported on the healing of gastrointestinal wounds made with the cautery. Klose and Rosenbaum-Canné believed that section by cautery produced more inflammation and delayed union than did division with knife. Their observations were made on 16 cats in which simple incisions were made through the wall of the stomach, these wounds being closed with various methods of suturing. Kopyloff studied the comparative healing of gastroenterostomies, the incisions being made with scissors, knife, and cautery, and sutured by different methods. His results led him to believe that cautery incisions caused pronounced inflammation and delayed healing. His work throws little light on the subject, however, since in the 8 animals in which cautery incision was done the specimens were removed between 25 and 180 days after operation. Only 1 early specimen was studied.

The healing of gastrointestinal wounds made with the scalpel or scissors, and the effect of using various suture materials and methods have been described amply by others. Martzloff and Suckow (9) in 1933 summarized the literature on wound healing in gastroenterostomy and reported observations on 44 dogs. They found that the most rapid healing was obtained by the use of a single layer of Halsted serosubmucosal resection sutures of silk. They were of the opinion that separate suture of the mucosa was unnecessary and actually retarded healing. Furthermore, sutures placed to evert the mucosa often caused epithelium to develop in the line of gastrointestinal apposition, resulting in adenomatous

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structures. Their findings indicate that healing takes place more rapidly when the mucosa is left unsutured.

PLAN OF STUDY

Twenty-seven full grown dogs were used. They were given only water for 24 hours preceding the operation. One hour before operation, morphine sulphate, 2 grains, was given hypodermically. Anesthesia was maintained with inhalation ether. In 17 animals an aseptic anterior gastroenterostomy was done and in 10 animals aseptic gastric resection was performed. The Waffler cautery was used to divide the stomach and intestine. After operation the animals were fed water the first day, milk the second, milk and gruel the third and fourth, and from then on, the standard dog chow. They were sacrificed with chloroform at from 1 to 3 day intervals from the 2d to 34th day. Specimens were removed while the animals were living, and were fixed in formalin. Segments were cut from the midportion of the anastomosis, embedded in paraffin, and the sections were stained with hematoxylin-eosin and van Gieson.

OPERATIVE PROCEDURE

The procedure used in these experiments was the same in principle as the one reported by Emile Holman. In the early experiments the gastric resections were done with the use of only Payr clamps at the line of transection, the suturing then being done over these same clamps. In the more recent experiments, the Payr clamp was replaced, after the wall was crushed, by either a Martzloff or a Wangensteen clamp. Another crushing clamp was applied distal to the anastomosis clamp and the intervening segment of stomach wall was divided with the Waffler cautery. A 3 millimeter cuff of tissue was left protruding beyond the clamp and this cuff was then seared for 15 seconds with the cautery. Reasons for leaving the cuff are given below. The jejunal stoma was made by excising with the cautery a segment of the antimesenteric wall protruding beyond an anastomosis clamp, again allowing the seared cuff to project 3 millimeters beyond the clamp. Preliminary crushing with a Payr clamp was not found to be necessary in the jejunum. In the simple gastroenterostomies the stomach opening likewise was made by excising a segment of the anterior gastric wall protruding beyond an applied anastomosis clamp, the same 3 millimeter cuff being left projecting beyond the clamp. An assistant held the anastomosis clamps while the sutures were placed.

The prevention of hemorrhage in closed anastomoses presented a problem which was solved after we had experimented with various means of treating the divided end of the stomach. It was found that crushing alone did not prevent bleeding. Furthermore, if one simply and rapidly cuts the stomach from the anastomosis clamp with the actual cautery, brisk hemorrhage may result when the clamps are withdrawn. Heating the anastomosis clamp with the Waffler cautery for 20 to 30 seconds will insure coagulation of the vessels, but this method has the disadvantage of damaging the contiguous stomach wall by heat transmitted from the clamp. The one fatality in the series occurred in an animal in which this method was used; death was due to localized peritonitis resulting from sutures giving way in an area damaged by transmitted heat. When the electrocoagulating unit was applied to the anastomosis clamp, it was found that high voltage for a long period of time was necessary to prevent bleeding, producing the same injury as did heating the clamp with the actual cautery.

These experiences led to the adoption of the method of leaving a 3 millimeter cuff of tissue protruding above the clamp when the stomach or intestine was resected. When the cuff was seared with the actual cautery at bright red heat for 15 seconds most effective hemostasis resulted, and damage to the tissues beneath the clamp was prevented. A study of early specimens showed that this cauterized cuff had disappeared almost entirely in 48 hours, probably from the action of the digestive juices. In no instance did it lengthen the flange or cause obstruction. The area crushed with the Payr clamp formed the granulating bed. The large vessels which approached the line of anastomosis were underrun with a silk suture on an intestinal needle and then tied.

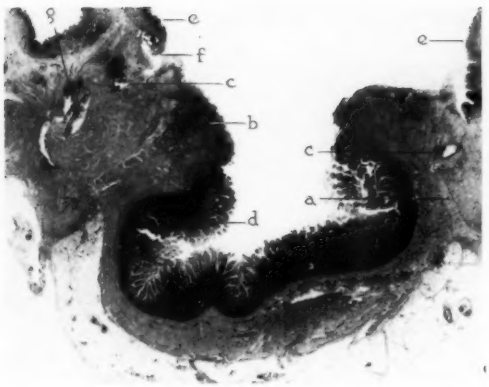

Fig. 1. Five day healing, Dog 25, gastroenterostomy: *a*, line of apposition; *b*, granulating bed covered with fibrinocellular membrane; *c*, chromic suture; *d*, intestine; *e*, stomach; *f*, single layer of epithelium beginning to grow over granulating bed, and marginal cysts; *g*, damage from silk suture.

Fig. 2. Nine day healing, Dog 22, gastroenterostomy: *a*, line of apposition; *b*, granulating bed; *c*, gland formation and marginal cysts; *d*, intestine; *e*, stomach; *f*, chromic suture.

Two different suturing methods were used in the series. In 10 animals 2 posterior rows of serosubmucosal interrupted mattress sutures of medium silk were first placed. The clamps were then rotated 180 degrees, an anterior row of Lembert sutures of medium silk was laid, and the clamps were withdrawn. A few sutures then were placed at the ends of the anastomosis to complete it. The agglutinated edges within were opened by digital manipulation. This method of suturing was found to be tedious and, at times, technically difficult. Sometimes it was impossible to rotate the clamps after the posterior rows had been placed without putting tension on the sutures. Furthermore, the posterior flange resulting from the use of this method was unnecessarily long.

In the 17 remaining animals, a continuous serosubmucosal suture of No. 00 chromic catgut on a small curved intestinal needle was used posteriorly directly beneath the clamps and parallel to them. The clamps were rotated and another suture of the same type was applied anteriorly. As the clamps were withdrawn the sutures were pulled taut and the two ends were tied. *This results in serosa to serosa approximation and an inverted free mucous membrane.* A single row of Lembert sutures was placed around the circumference, thus completing the anastomosis. This technique was described by Martzloff and Burget (7) for aseptic intestinal anastomosis and has been adopted recently by Wangensteen (15). It has the same features as the Parker-Kerr suture except that it remains as the inner layer in the anastomosis. It was found to be rapid and simple, and it permitted free rotation of the clamps.

Immediately following the completion of the anastomosis the stomach was washed with tap water by means of an indwelling stomach tube to determine the degree of bleeding. The wash water either returned clear or had a slightly pink color; nothing indicative of even moderate bleeding was observed in any instance. Late hemorrhage was not noted in any of the animals. The omentum was laid over the suture line after the anastomosis was replaced in the abdomen.

GROSS APPEARANCE OF THE SPECIMENS

Usually only the omentum was found adherent to the suture line. The serosa healed with a minimal degree of reaction. In none of the specimens was the afferent or the efferent stoma encroached upon sufficiently to cause obstruction. Also, it is significant to note that none of the animals showed signs of postoperative obstruction.

The 3 day specimens showed a uniform gap of 3 to 5 millimeters between the edges of

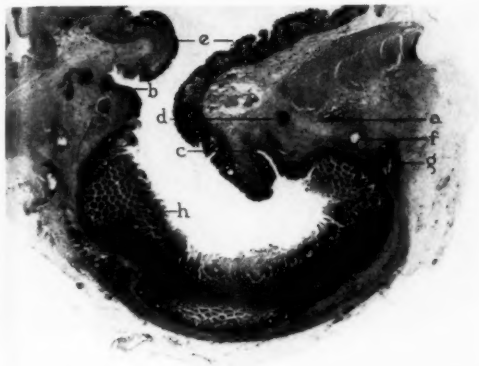

Fig. 3. Eleven day healing, Dog 24, gastroenterostomy; *a*, line of apposition; *b*, granulating bed; *c*, mucous membrane covered by single layer of epithelium; *d*, granular débris; *e*, stomach; *f*, chromic suture; *g*, silk suture; *h*, intestine.

mucous membrane. The bed of this mucosal defect was covered with necrotic débris. By the tenth day the gap measured 1 to 2 millimeters. In 14 to 17 days the mucous membranes lay in apposition. A notable finding was the uniformity in width of the mucosal defect. Only a few early specimens showed much variation in diameter of the unhealed portion in different areas.

HEALING OF THE MUCOUS MEMBRANE

The 3 day specimens showed no definite regrowth of epithelium. By the fifth day a single layer of mucosal cells had started to grow over the granulating bed. In the 6 day specimen these cells had advanced further between the pyogenic membrane and the granulating bed, about an equal distance from the intestine as from the stomach. Marginal cysts were present on the stomach side, but not on the intestinal side, at this time. By the 9th day the mucosal defect had diminished greatly in width and one had the impression that this was not due as much to epithelial regeneration as to contraction of the granulating bed. This 9 day specimen showed the formation of three marginal cysts on the stomach side. At the margin of the intestinal mucous membrane there was definite gland formation and the single layer of epithelium projecting therefrom showed secreting cells.

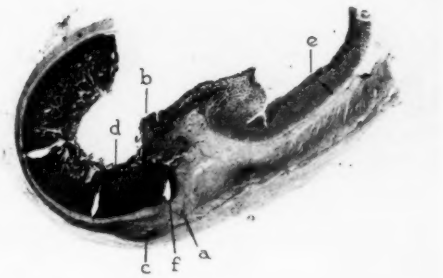

Fig. 4. Fourteen day healing, Dog 2, gastric resection: *a*, line of apposition; *b*, mucous membrane in contact; *c*, silk suture; *d*, intestine; *e*, stomach; *f*, healing by single layer of epithelial cells.

In one area of an 11 day specimen the mucous membrane was bridged by a single layer of epithelium, flanked by regenerated glands. One 14 day specimen showed complete coverage with a narrow zone of single layer epithelium. In the other 14 day specimen a 2–3 millimeter defect covered with a fibrinocellular membrane was still present. The 10 specimens between 17 and 34 days were epithelialized. By the 21st day the glands were well formed at the site of union.

LINE OF APPOSITION

The usual microscopic picture of the healing at the line of apposition was a proliferative one. None of the specimens showed abscess formation except around sutures. There was a scarcity of inflammatory cells in the early

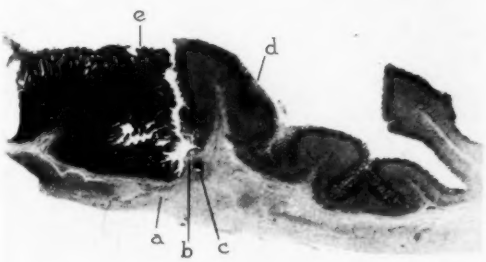

Fig. 5. Eighteen day healing, Dog 5, gastric resection: *a*, fibrous tissue at line of apposition; *b*, healing by single layer of epithelium; *c*, silk suture; *d*, stomach; *e*, intestine. Small flange.

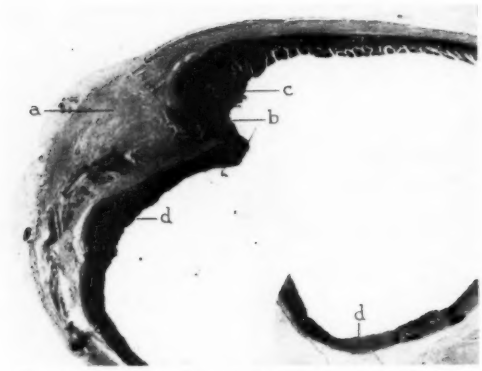

Fig. 6. Twenty-one day healing, Dog 11, gastroenterostomy: *a*, scar at line of apposition; *b*, healed mucous membrane with gland formation; *c*, intestine; *d*, stomach.

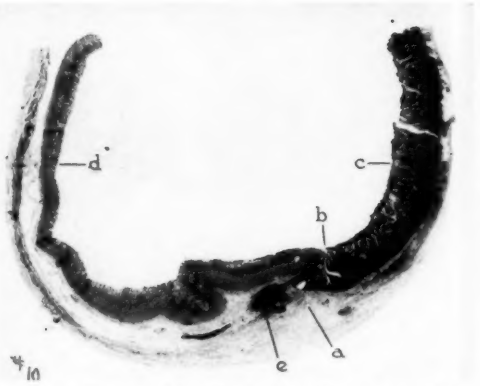

Fig. 7. Twenty-eight day healing, Dog 10, gastric resection: *a*, scar at line of apposition; *b*, mucous membrane with glands at site of union; *c*, intestine; *d*, stomach; *e*, area of lymphoid hyperplasia. Note absence of flange.

stages of healing except near the base of the granulating bed. By the eleventh day the line of serosal union was replaced by a zone of fibrous tissue in which the frayed ends of the muscularis could be seen.

SIZE OF THE FLANGE

Beginning with the 14 day specimens there was a definite decrease in the height of the flange. By the 18th day it was considerably smaller and in twenty-eight days the site of union was represented only by an area of slight thickening. It would appear that irritation from a granulating bed has something to do with maintaining the flange, for as soon as it was covered with mucosa the flange regressed.

MICROSCOPIC DESCRIPTION OF REPRESENTATIVE SPECIMENS

Figure 1. 5 days—Dog 25—gastroenterostomy. The line of apposition showed a minimal inflammatory response. A broad granulating bed was present, covered by a fibrinocellular membrane. The chromic suture was surrounded by a collection of polymorphonuclear leucocytes. On the stomach side of the defect the epithelium had begun to grow out as a single layer. On the intestinal side the epithelium also had begun to cover the ulcer, but there was less growth than from the stomach side. The mucous

Fig. 8. Thirty-two day healing, Dog 9, gastric resection: *a*, line of apposition; *b*, healed mucous membrane with glands; *c*, intestine; *d*, stomach.

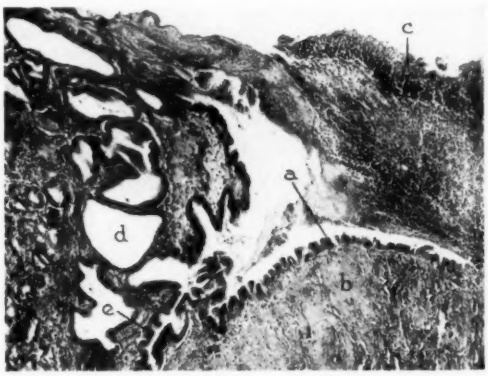

Fig. 9. Six day healing, Dog 12, gastroenterostomy: High power photomicrograph showing: *a*, single layer of epithelial cells growing from stomach side; *b*, granulating bed; *c*, fibrinocellular membrane; *d*, marginal cysts; *e*, early gland formation.

membrane adjacent to the defect showed some edema and cellular infiltration.

Figure 2. 9 days—Dog 22—gastroenterostomy. The line of apposition was filled with a thin layer of fibrin in which there were only scattered leucocytes. The granulating bed was about one-third the diameter of the 5 day specimen. The epithelial growth on the stomach side showed early gland formation and 3 marginal cysts. There was about an equal amount of epithelial regrowth and gland formation on the intestinal side.

Figure 3. 11 days—Dog 24—gastroenterostomy. The line of apposition was practically obliterated by a fibrous tissue zone. Some granular débris was present in this region. On one side the epithelium had grown over the entire granulating bed, being joined in the center by a narrow area of single celled epithelium. In another area the mucous membrane had not healed, the appearance being that of a 7 day specimen. Well defined gland formation was present.

Figure 4. 14 days—Dog 2—gastric resection. The line of apposition was replaced by fibrous tissue. The mucous membrane lay in apposition. There was definite gland formation, especially on the stomach side of the anastomosis. The granulating bed was covered by a single layer of epithelium. A silk suture in the muscularis was surrounded by a collection of polymorphonuclear cells. The flange was smaller than the earlier specimens.

Figure 5. 18 days—Dog 5—gastric resection. The line of apposition was demarcated by a zone of fibrous tissue in which the frayed ends of the muscle could be seen. The mucous membrane was healed by a single layer of epithelium. A silk suture surrounded by inflammatory cells lay near the healed mucous membrane. The flange was barely present.

Figure 6. 21 days—Dog 11—gastroenterostomy. The mucous membrane had healed completely with definite gland formation at the juncture. A small flange was present.

Figure 7. 28 days—Dog 10—gastric resection. The mucous membrane had healed completely with gland formation at the point of union. An area of lymphoid hyperplasia was present in the muscularis of the stomach. The flange was represented by an area of slight thickening.

Figure 8. 32 days—Dog 9—gastric resection. The microscopic appearance was similar to the 28 day specimen.

Figure 9. 6 days—Dog 12—gastroenterostomy. The gross and microscopic picture was about the same as the 5 day specimen. A high power photomicrograph is shown to illustrate the manner in which the new single layer of epithelium grows on granulating bed beneath fibrinocellular membrane.

HEALING PROCESS IN CLOSED ANASTOMOSES COMPARED WITH OPEN METHODS

The rate and manner of healing of gastrointestinal wounds made aseptically with the actual cautery compare favorably with other methods. The aseptic procedures used in these experiments apparently will result in mucosal healing in 14 to 17 days, while portions of the anastomosis may be epithelialized in eleven days. There are ample opportunities to compare these results with the findings of others who have experimented with open anastomoses. Gould, for example, found that the average time for mucosal healing in experimental gastrointestinal anastomoses was 14 days. Flint came to the same conclusion after studying comparative rates of healing with the use of three different methods of suturing. The more comprehensive study by Martzloff and Suckow (9) showed healing in 6 days in 2 anastomoses in which Halsted presection sutures were used. When the same authors used the Connell suture they found epithelialization by a single layer in one 14 day specimen and incomplete coverage in another. They also reported mucosal union in one of two 14 day specimens in which the commonly employed continuous hemostatic suture was utilized. Healing with this method, however, was attended by intense inflammatory reaction, irregular mucosal defects, and frequent inclusion cysts.

When healing at the line of apposition is used as a yardstick, the closed method compares to even better advantage. The fact that all of the specimens showed the healing process to be a proliferative one attests to the advantage of preventing soiling by the use of an aseptic procedure.

CONCLUSIONS

1. The healing in 17 aseptic anterior gastroenterostomies and 10 aseptic gastric resections, experimentally produced in dogs, was studied.

2. Hemorrhage was most effectively prevented by leaving a seared 3 millimeter cuff of tissue protruding above the clamp after resection of the stomach or intestine had been carried out.

3. The mucous membrane healed in 14 to 17 days.

4. The usual microscopic picture of the healing at the line of apposition was a proliferative one.

5. The flange began to decrease in height at the 14th day and was represented by an area of slight thickening in 28 days.

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RENAL DYSFUNCTION IN PROSTATISM

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INDIVIDUALS suffering from prostatism often have renal function which is definitely though not irreparably damaged. That is to say, after varying periods of uninterrupted vesical drainage, renal function materially improves. What then is the portion of the kidney that is not irreversibly impaired by the urethral obstruction? Is the primary effect on the tubule, the glomerulus or both? An attempt to localize the pathological condition in partial reversible renal dysfunction constitutes the essence of this dissertation.

In order to ascertain the site of this renal pathological physiology it was considered imperative that some means be employed to make quantitative estimates separately of the function of the glomerulus and the tubule. Two such tests have been described: inulin clearance for the determination of glomerular function and phenol red clearance as an index of tubule activity.

Clinical material. The 6 patients used in this study were selected at random from the Urological Service of the Louisville City Hospital. The patients varied in age from 52 to 78 years, had symptoms of prostatism for more than 2 years, and presented no evidence of any nephritic lesion.

Before each functional study the patients were hydrated so that their urinary output was not less than 1.0 cubic centimeter per minute. Simultaneous clearance tests (inulin and phenol red) were done on 3 occasions in all but 1 individual. The clearance tests were done intermittently during the preoperative vesical drainage period which varied from 6 to 16 days. The interval at which these tests were executed was determined by the patients' general clinical appearance and improvement.

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Experimental method. Inulin (10 grams) dissolved in 100 cubic centimeters of normal saline at 37.5 degrees C. was injected intravenously at the rate of 10 cubic centimeters per minute. Thirty minutes later 0.5 gram of phenol red dissolved in 50 cubic centimeters of weak sodium bicarbonate solution was injected intravenously at the same rate as the inulin; the dye was injected later so that an adequate serum concentration could be maintained.

One hour after the completion of the inulin injection all the urine was emptied from the bladder per catheter and discarded. At the same time 15 cubic centimeters of blood, which was the second specimen, was taken from the antecubital vein; the first having been taken before the initiation of the experiment. Two other blood specimens were taken later, that is at 2 and 3 hours after the completion of the inulin injection. Blood samples were not taken during the first hour since this is the period of equilibration between the plasma, tissues and injected clearance substances (Alving and Miller).

Urine specimens were collected for analysis at 1½, 2½, and 3½ hour intervals following the completion of the inulin injection. The method of collecting the urine was carried out in the following manner: all the urine was allowed to drain from the bladder which was then washed out with three 30 cubic centimeter portions of saline followed by distention with air to insure complete emptying.

The clearance rates for both substances were calculated at hourly intervals following completion of the inulin injection which constituted the zero point of clearance time. Since the samples of urine and blood were collected at alternating half hourly intervals, the clearance values were ascertained by interpolation.

The clearance rate was determined by the usual formula $C = UV/B$. C = cubic centimeters of plasma cleared of inulin or phenol red per minute; U = urine inulin or phenol red con-

TABLE I.—RESULTS OF EXPERIMENTS

Case No.	Days of catheter drainage	Duration of clearance test (hrs.)	Inulin clearance	Phenol red clearance	Phenol inulin/red ratio
1 79746	0	1.0	112	260	2.3
		2.0	120	263	2.1
		3.0	106	244	2.2
	6	1.0	118	359	3.0
		2.0	127	370	2.9
		3.0	120	381	3.1
	10	1.0	101	302	2.9
		2.0	107	324	3.0
		3.0	93	289	3.1
2 63707	0	1.0	122	270	2.2
		2.0	113	262	2.1
		3.0	119	276	2.3
	6	1.0	129	400	3.2
		2.0	134	381	2.9
		3.0	140	397	2.9
	10	1.0	123	376	3.0
		2.0	117	360	3.0
		3.0	127	370	2.9
3 42772	0	1.0	96	168	1.7
		2.0	90	*	
		3.0	88	172	1.9
	6	1.0	89	224	2.5
		2.0	97	228	2.3
		3.0	101	239	2.3
	13	1.0	116	291	2.5
		2.0	121	302	2.5
		3.0	110	286	2.4
4 61903	0	1.0	110	220	2.0
		2.0	98	232	2.3
		3.0	104	223	2.1
	6	1.0	120	340	2.8
		2.0	117	358	2.8
		3.0	115	339	2.8
5 51071	0	1.0	114	260	2.2
		2.0	102	234	2.2
		3.0	*	241	
	7	1.0	130	347	2.6
		2.0	141	332	2.3
		3.0	119	329	2.5
	14	1.0	96	250	2.6
		2.0	91	240	2.5
		3.0	104	261	2.5
6 80372	0	1.0	101	180	1.9
		2.0	96	167	1.7
		3.0	90	150	1.6
	8	1.0	99	212	2.1
		2.0	111	193	1.7
		3.0	92	201	2.1
	16	1.0	103	217	2.1
		2.0	111	201	1.8
		3.0	110	213	1.9

*Blood sample hemolyzed.

centration in milligrams per cent; B = mean plasma inulin or phenol red concentration per cent; and V = urine volume in cubic centimeters per minute.

The method of measuring quantitatively the amount of inulin in plasma and urine was that described by Corcoran and Page. In principle this method makes use of the fact that a blue compound results from the combination of diphenylamine and a polysaccharide in the presence of hot concentrated hydrochloric acid. Colorimetric readings were made, a single cell compensating photoelectric colorimeter of Evelyn, and No. 620 filter being used.

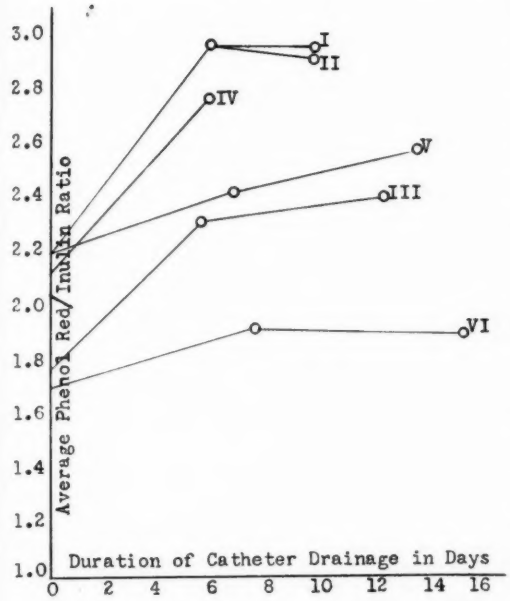
TABLE II.—COMPARISON OF PHENOL RED AND INULIN CLEARANCES

Case number	Mean percentage increase of inulin clearance following drainage	Mean percentage increase of phenol red clearance following drainage
1	26.2	41.8
2	19.0	38.1
3	32.1	36.3
4	20.0	41.7
5	5.5	27.1
6	6.0	19.2
Average	16.46	33.86

Phenol red determinations were made colorimetrically and the same type of photoelectric colorimeter with a No. 520 filter was used. A standard curve was first prepared, the known concentrations of dye solutions being used, and the unknown experimental concentration was read directly from the curve.

In the execution of phenol red clearance tests there are several essential points. The plasma concentration of the dye must be maintained at a level below 1.0 milligram per cent. When plasma dilutions are made the alkali must never be added to the plasma until after dilution, otherwise precipitation will result with its concomitant false colorimetric values. The inherent chromogenic properties of the plasma must be compensated for in the colorimeter and each sample of plasma must be tested for hemolysis (Bing and Baker).

Interpretation of the experimental results. The tabulated results (Table I) demonstrate that continuous vesical drainage improves total renal function in prostatism. However, no apparent relationship between the length of vesical drainage and the amount of renal functional improvement could be demonstrated. That is, improvement was dependent upon the amount of actual damage that occurred before the establishment of drainage, and this no doubt must be dependent upon the duration of symptoms. Case 6 (Table I) with its limited functional improvement, though drainage was continuous over a 16 day period, suggests this conclusion.



Graph 1. Total renal function continues to a certain point and then ceases.

The phenol red/inulin ratio was incorporated in the table since it more accurately represents renal function (Goldring, Clarke and Smith). The normal phenol red/inulin ratio is 3.3. That the ratio more nearly represents the true index of renal activity was demonstrated in Case 1 (the third hour of the clearance rate period on the tenth day of catheter drainage). Here it is seen that the clearance rate for inulin is 93 cubic centimeters per minute (normal 125 c.c.) and the phenol red clearance is 289 cubic centimeters per minute (normal 400 c.c.). These two figures would seem to indicate markedly impaired renal function though when the phenol red/inulin ratio is examined it is found to be 3.1 as compared to 3.3 which is normal. Hence, renal function is in this particular instance not impaired as seriously as one would be led to believe by examining the clearance rates separately.

Upon examination of Table II it is seen that phenol red clearances seem to have improved relatively more than the inulin clearance. From these figures the improvement of the tubule function, as compared with that of the glomerulus, occurred in a ratio of approximately 2:1. Obviously to establish this as factual a larger series of cases will have to be investigated. It can be said then, in the final analysis of the experimental results obtained in this study, that renal function was improved following prolonged periods of vesical drainage in prostatism and that the increase was apparently more pronounced in the tubule than the glomerular elements of the kidney.

Graph 1 demonstrates that the improvement of total renal function continues to a certain point and then ceases; that is, apparently renal damage is reversible to a certain point and after that is irreversible. Just what determines the degree of irreversibility was not determined. However, this factor of reversibility of renal functional damage has long been appreciated by urologists and the stationary period (the plateaus on the graph) has been loosely termed "renal stability" and constitutes one of the principal criteria indicative of the optimum time for prostatectomy.

EVALUATION OF STUDY

The problem of renal dysfunction in prostatism has received little or no experimental investigation. In fact, careful search of the literature reveals no single reference dealing with this problem. Reference was made on occasion to the observed fact that renal function improved in prostatism with the institution of bladder drainage, but further than advocating this observation as significant as an operative index nothing could be found.

Strong studied the nephron by microdissection in experimental hydronephrosis and found that early in hydronephrosis the proximal convoluted tubule became markedly reduced in volume. Suzuki, using vital stains, found cells of the distal portion of the proximal convoluted tubules to be damaged before those in the initial portion of the tubule. Hinman, working with rabbits, found that the tubule suffered damage before the glomerulus. In these various experiments, the urinary back pressure, though created by different means was still in its early stages and from that point of view one might imagine, at least, that the situation was somewhat comparable to the urinary obstruction of prostatism, and it is of

interest that the results of this work support these findings.

SUMMARY

1. Renal dysfunction was investigated by the use of simultaneous inulin and phenol red clearance tests.

2. Renal dysfunction in prostatism is primarily a tubule dysfunction.

3. The disturbed renal function in prostatism is definitely improved by continuous vesical drainage.

4. Renal damage due to prostatism is partially reversible. Re-establishment of renal function is not complete, but reaches a peak beyond which no further functional improvement occurs.

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THE EFFECT OF HEPARIN ON THE BEHAVIOR OF INFARCTION OF THE INTESTINE:

An Experimental Study

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IN his recent reports (3, 4) Murray advocates the use of heparin following resection for infarction of the intestine. These reports have stimulated our attempt to determine the effect of this anticoagulant upon various types of mesenteric vascular occlusions and strangulations. The high postoperative mortality in cases of mesenteric vascular occlusion has been ascribed to the propagation or extension of small thrombi into larger vessels after operation. The question arises as to the value of heparin in enhancing the viability of the intestine whose circulation has been compromised by mesenteric vascular occlusion. Our experiments were conducted to study this problem and to determine under what conditions it is safe to administer heparin.

METHOD

The circulation of the small intestine of the dog was impaired in 4 ways: (1) ligation of mesenteric vessels, (2) the injection of 2 per cent sodium ricinoleate[1] into the mesenteric vessels to produce slow thrombosis, (3) the injection of fibrinogen[2] into the mesenteric vessels to produce rapid coagulation, and (4) strangulation of loops of intestine. Heparin[3] was administered in some instances before the lesions were produced, and shortly afterward in others. In each instance a control series of experiments was conducted, in which no heparin was administered.

Heparinization was maintained for varying periods of time up to 7 days. The multiple injection method was used, except in a few instances in which continuous venoclysis was administered overnight. The coagulation time was kept well above normal, but little effort was made to stabilize it at a constant level. It apparently made little difference in the results whether the coagulation time was slightly above normal or far above. A control coagulation time was taken before each experiment. Coagulation times after the administration of heparin varied from 10 to 45 minutes.

From the Division of Surgery, Northwestern University Medical School.

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[1] Soricin, 2%.

[2] Fibrogen. Tissue fibrinogen and cephalin in sterile suspension with merthiolate (sodium ethylmercuri thiosalicylate 1: 10,000).

[3] Liquaemin (Roche-Organon).

EXPERIMENTS CONCERNED WITH LARGE MESENTERIC VESSELS

In the first series of experiments the superior mesenteric vessels were ligated. The results of such ligations have been reported many times in the past. Scott and Wangensteen found that the average length of life following ligation of the superior mesenteric vein in dogs was 5½ hours; following ligation of the superior mesenteric artery, 20 hours; and following ligation of both artery and vein, 19 hours. The results of control experiments were comparable to theirs.

The process of actual infarction is reversible up to 2 to 4 hours following ligation of the superior mesenteric vein, and the animal usually survived if large quantities of blood were given by transfusion and the ligature released within this period of time. The blood volume ordinarily was reduced 50 to 60 per cent. Heparin, as might be expected, had no effect on the course of such animals. Because of the wide variation in survival times of control animals, it was difficult to ascertain whether heparin actually hastened death by prolonging the coagulation time and allowing the animal to bleed more freely.

Ligation of the superior mesenteric artery in heparinized dogs produced the same end-results as in the control series.

TABLE I.—EXPERIMENTS CONCERNING SMALLER MESENTERIC VESSELS

Procedure	Heparinized dogs	Result	Control dogs	Result
Devascularization of 10 to 12 cm. small intestine by ligation	3	All survived; smooth adhesions	3	Death in 2 from gangrene and peritonitis in 48 and 70 hrs. One survived; extensive adhesions
Devascularization of 15 to 20 cm. small intestine by ligation	3	Death in 72 hrs., 4 days and 5 days respectively	2	Found dead after 24 and 48 hrs.
0.5 c.c. 2% sodium ricinoleate injected into medium sized arteries; arches ligated on each side	5	One died after 48 hrs.; 4 survived	4	Death in 2 within 48 hrs.; (gangrene). Resection of gangrenous segment done in 2 after 24 hrs.; 1 died from peritonitis
1 c.c. fibrinogen injected into medium sized arteries; arches ligated on each side	4	Death within 12, 24, 24 and 48 hrs. respectively; (gangrene)	3	Death within 8, 12, and 24 hrs. respectively (gangrene)

Rapid thrombosis of the superior mesenteric vein was produced by placing a rubber-guarded clamp on the vein near the junction with the portal vein. Five cubic centimeters of fibrinogen was then injected into the superior mesenteric vein distal to clamp, and the clamp removed in 20 minutes. The mesenteric vessels became obstructed by a thick coagulum. The course of such animals was similar to that of those in which ligation was done. Heparin had no influence on the lesion.

Slow thrombosis of the superior mesenteric vein was produced by injecting 0.5 cubic centimeters of 2 per cent sodium ricinoleate solution distal to a rubber guarded clamp as described. When the clamp was removed after 20 minutes, the cyanotic, relaxed appearance of the intestine due to clamping, rapidly disappeared with the onset of hyperperistaltic contractions. A return of color gave one the impression that viability was assured. The abdominal wall was then closed. However, a thrombus formed within the damaged vessel, propagated postoperatively, and caused death within 24 to 48 hours. Postmortem examination revealed massive hemorrhagic infarction of the intestine due to thrombosis of the superior mesenteric and portal veins.

In 3 of 5 such animals in which heparinization was maintained for 5 to 7 days, thrombosis was prevented, and they lived with no apparent ill-effects. The 2 other dogs died in 48 and 60 hours with hemorrhagic infarction of the intestine. In 2 other animals the administration of heparin was stopped after 24 hours, and these animals died several hours later from infarction due to mesenteric thrombosis. Apparently the heparin had not been continued for a long enough period of time to prevent eventual thrombosis and death.

EXPERIMENTS CONCERNED WITH SMALLER MESENTERIC VESSELS

Welsh and Mall demonstrated that if more than 5 centimeters of intestine are deprived of blood supply, gangrene results. Similarly, Eisberg found that in the dog's intestine there is sufficient inosculation of the intramural vessels in the longitudinal axis to supply at least 5 centimeters of uncontracted intestine if the vasa recta to such a segment are obstructed. In order to deprive a longer segment of its blood supply, care must be taken to ligate all vessels from adjoining vascular arches, including those immediately adjacent to the serosa, as well as main vessel to that segment.

When the vessels supplying 10 to 12 centimeters of intestine were ligated, 2 of 3 control animals died from gangrene of the segment and peritonitis in 48 and 70 hours, respectively. The third showed no apparent ill effects. The 3 animals treated with heparin for 5 days all lived and remained well. Subsequent laparotomy on the surviving untreated animal showed more extensive adhesions than in the animals treated with heparin. The anticoagulant thus permitted the survival of a segment of bowel 10 to 12 centimeters in length after occlusion of its extramural blood supply. The death of the control animals confirms the fact that in the dog a segment of bowel 10 or 12 centimeters in length usually cannot survive when devascularized. It is possible that the anticoagulant, by preventing thrombi from forming in the intramural vessels, allows for more extensive collateral cir-

TABLE II.—STRANGULATION EXPERIMENTS

Control series			Heparin series		
Time strangulated hrs.	Length of intestine ft.	Result	Time strangulated hrs.	Length of intestine ft.	Result
3	1	Recovery	3	1	Death. Hemorrhage. 24 hrs. (found dead)
3	1	Death. Peritonitis due to evisceration 72 hrs.	3	1	Recovery
6	1	Recovery	6	1	Death. Hemorrhage. 24 hrs. (found dead)
6	1	Recovery	6	1	Death. Hemorrhage, perforation and peritonitis. 24 hrs. (found dead)
3	2	Recovery	3	2	Death. Hemorrhage. 24 hrs. (found dead)
3	2	Recovery	3	2	Death. Hemorrhage. 24 hrs. (found dead)
6	2	Recovery	6	2	Death. Hemorrhage. 24 hrs. (found dead)
6	2	Recovery	6	2	Death. Hemorrhage. 12 hrs.
6	2	Recovery	6	2	Death. Hemorrhage. 12 hrs.

culation from the normal bowel on either end. If increased bleeding occurs following heparin, apparently the blood loss from a short segment before recovery sets in is not sufficient to cause death.

When the vessels supplying 15 to 20 centimeters of small intestine were ligated, heparinization did not permit the survival of the segment, although these animals lived somewhat longer than did the control animals. All died within 5 days with gangrene of the deprived segment and peritonitis. None of the control animals lived longer than 48 hours, while the survival periods of the 3 heparinized dogs were 72 hours, 4 days, and 5 days, respectively. Blood loss was no doubt increased, but did not account for death in these animals. This experiment would indicate that a segment of bowel of 15 to 20 centimeters is apparently too long to allow collateral blood supply to nourish the entire segment from either end when the extramural blood supply is cut off.

Slow thrombosis of medium sized mesenteric vessels was produced by the injection of 0.5 cubic centimeter of 2 per cent sodium ricinoleate into such an artery distal to a clamp which included both artery and vein. This resulted in spasm of the involved segment of bowel, already cyanotic from the clamping. Removal of the clamp after 20 minutes was immediately followed by an apparent return to normal color. Palpation revealed pulsations in the vasa recta, and hyperperistalsis was marked. It seemed that the bowel would survive. However, each of 4 such dogs showed infarction of the segment within 24 hours, and, unless the segment was resected, died within 48 hours.

The same experiment was carried out on 5 dogs which were heparinized at the time of injection and kept heparinized for 5 days. Four of the 5 animals survived. When the surviving dogs were reopened 1 or 2 weeks later, the omentum and neighboring intestinal loops were found closely adherent to the involved segment and its mesentery.

Rapid thrombosis of medium sized mesenteric vessels was produced by injecting 2 cubic centimeters of fibrinogen distal to a clamp, as described. Although a coagulum formed within the vessels within a few minutes, the survival times of 3 such animals varied from 8 to 24 hours. The 4 heparinized animals in which this procedure was done lived from 12 to 48 hours. Heparinization may have thus prolonged life to a certain extent, but did not prevent infarction and death in animals in which rapid thrombosis was produced.

STRANGULATION EXPERIMENTS

Scott and Wangensteen found that the length of bowel involved in strangulation is a factor in determining the survival period. Aird and others have emphasized other factors which play important rôles in the cause of death following low intestinal strangulation obstructions. It has been shown that in

short-loop strangulations death is usually due to perforation and peritonitis; in strangulations of medium length death is apparently due to the absorption of certain toxins; in long-loop strangulations death is due to diminution in blood volume resulting from blood loss into the lumen and wall of the strangulated intestine and into the peritoneal cavity.

Our strangulation experiments were concerned with determining the effect on the recovery of medium lengths of gut strangulated for varying periods of time up to 6 hours. It was felt that release of the strangulation within this period would not allow the lethal factors associated with low intestinal strangulation obstruction to be effective.

Four groups of strangulations were carried out by means of binding tape (Table II). In each group a control series of dogs was compared with a heparinized series. Fasting dogs of about the same weight were used, and an attempt was made to produce the same amount of vascular obstruction in each instance. The tape was first tied around the mesenteric stump and then around the loop of ileum to be obstructed, and was pulled as tightly as the tape would allow.

In most instances, when the tape was released after at least 3 hours, the bowel appeared questionably viable. In others, the infarction appeared irreversible. The bowel resembled that of the human during operations for strangulated hernia after incarceration for 12 hours or more. The segment was dark blue or black until released. It then became very red with purple or bluish areas in the wall, and the lumen contained blood. The peritoneum contained a bloody transudate.

All but one of the control animals recovered after release of the strangulation and closure of the abdomen. The 1 death occurred after 72 hours and was due to peritonitis brought about by evisceration before strangulation was released. All but 1 of the heparinized dogs were found dead 24 hours after release of strangulations and closure of abdomen.

The cause of death in these animals was undoubtedly shock due to blood and fluid loss as evidenced by the large amount of bloody fluid in the peritoneal cavity and in the lumen of the bowel. However, in one of the 6-hour, 1-foot strangulations, death was due to perforation and peritonitis. The prolonged coagulation time following heparin apparently allowed free bleeding, thus increasing the amount of blood lost during the strangulation.

An observation was made during the strangulation experiments concerning the use of hot laparotomy pads in cases of questionable viability of the intestine. We wished to determine the safety of administering heparin after operation in such cases when resection was not done. Each of 4 dogs in which the bleeding points on a strangulated loop were controlled by means of hot laparotomy pads, died from hemorrhage after heparin was administered. It was observed that the previously coagulated bleeding points began to bleed within 1 hour after injection of heparin.

RESECTION

We have performed several resections in the presence of heparinization. There was much more bleeding than is normally encountered, and much time was consumed for hemostasis. However, the procedure was satisfactorily completed in each case, and the mortality following resection was no different than in control animals.

CONCLUSIONS

From our experiments it would seem that it is unsafe to administer heparin after operation in cases of impaired circulation of the intestine when resection is not performed. Although it appears that heparin enhances the chance of recovery of short devascularized segments, in cases of mesenteric vascular occlusion or strangulation it should be reserved only for those cases in which resection is performed.

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EXTRATHYROIDAL METABOLISM OF IODINE

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IODINE has been identified with the physiology of the thyroid gland since the findings of Chatin, Baumann, Marine, and others. These studies have tended to focus attention on the intimate rôle played by thyroid tissue in iodine metabolism. Reports of subsequent work on the function of iodine in the organism, for the most part, have assumed or implied the participation of thyroid tissue.

The recent experimental *in vitro* production of thyroxine or thyroxine-like substances by the iodization of protein has been accomplished. In view of the formation of these calorigenic substances in the absence of thyroid tissue, the effect of iodine on the completely thyroidectomized animal should be significant. The results of such observations form the basis of this report.

METHODS OF STUDY

For this investigation 42 male, albino rats aged 7 weeks and weighing approximately 165 grams were selected and divided into 2 groups. Twenty-four rats on which thyroidectomy was not performed formed 1 group and 18 thyroidectomized rats formed a second group. Thyroidectomy was complete in all animals but one in which a small amount of thyroid tissue was observed at necropsy.

All animals received the same goitrogenic, low iodine diet described by Remington, and all animals had free access to distilled water.

The groups of intact and thyroidectomized animals were each divided in half; 12 intact and 9 thyroidectomized animals each formed a group which received an iodine supplement. This was administered in the drinking water, 1.5 micrograms of iodine as potassium iodide per cubic centimeter of water, which supplied to these 2 groups, respectively, an average iodine intake of 34 and 27 micrograms per rat per day. Less than 5 per cent difference in the intake in the 2 groups existed, calculated on a basis of average body weight. Thus 4 groups of animals were arranged: 2 groups of intact animals, 1 receiving a supplement of iodine and the other on a low iodine intake; and similarly, 2 groups of thyroidectomized animals on supplemented and restricted iodine intake.

Body weights were recorded every third day and the consumption of food and water was measured and recorded daily. Respiratory metabolism was determined twice during the course of the experiment.

EXPERIMENTAL DATA

The data have been calculated and expressed in terms of unit weight and surface area of rat tissue because of the diverging weights of the different groups. Thus the food intake of a group of rats averaging 200 grams was compared properly with the food intake of a group averaging 150 grams.

Food and water intake and changes in body weight were observed from the fourth to the sixty-ninth postoperative day, thus constituting a 65 day experimental period.

The changes in surface area of these animals (Fig. 1) were based on the percentage change in weights from the onset of the experiment. Difference in the level of iodine intake made little change in the rate of growth of intact animals, but in thyroidectomized animals differences were observed. Those on restricted iodine intake lost weight and surface area more rapidly than the animals receiving the iodine supplement. The terminal rise of the growth curve (Fig. 1) in the thyroidectomized animals on low iodine intake is explained by the death of low weight members of this group, whereas the animals whose percentage loss of surface area was less survived.

A portion of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Doctor of Philosophy. This study, combined with the essay "The Relation of the Thyroid and the Pituitary Glands to Iodine Metabolism," was awarded the Van Meter Prize by the Association for the Study of Goiter.

Work done at the Institute of Experimental Medicine under the direction of Dr. G. M. Higgins.

Presented in the Forum on Fundamental Surgical Problems, Clinical Congress of the American College of Surgeons, Boston, November 3–7, 1941.

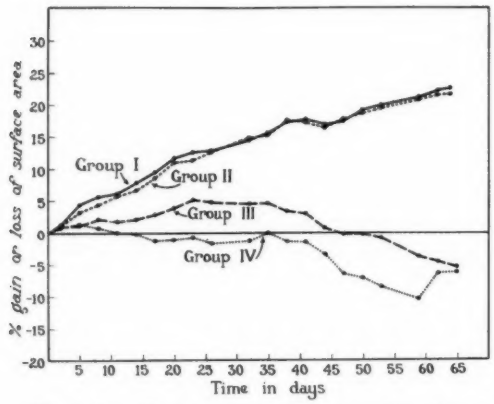

Fig. 1. Growth curves expressed as percentage changes in surface area. •——• Group I, intact animal, adequate iodine intake; ○----○ group II, intact animal, low iodine intake; •– –• group III, thyroidectomized animal, adequate iodine intake; ○·····○ group IV, thyroidectomized animal, low iodine intake.

The actual changes in weight and surface area of the 4 groups (Table I) included the changes occurring during the life of the rats which died during the course of the experiment. These figures represent the net performance of the groups more accurately than the graph of percentage changes but they do not show the progressive changes so well. Again there was noted very little difference in the changes in weight or surface area in the 2 groups of intact animals receiving low and adequate iodine intake. But of the thyroidectomized animals, those receiving the low iodine diet without iodine supplement suffered a threefold loss of weight and surface area in comparison with those animals in the thyroidectomized group receiving an iodine supplement.

The food intake and the gain or loss of surface area in proportion to the food consumed were computed (Table II). The latter comparison represents a measure of food utilization. The food intake and its utilization by the 2 groups of intact animals were approximately the same. However, among the thyroidectomized animals, although those receiving a low

TABLE I.—CHANGES IN WEIGHT AND SURFACE AREA THAT OCCURRED DURING THE EXPERIMENTAL PERIOD.

Animals	Groups	Actual gain or loss over total period*		Average gain or loss per rat per day	
		Wt., gm.	Surface, sq. cm.	Wt., gm.	Surface, sq. cm.
Intact	I Adequate iodine	+930	+796	+1.21	+1.03
	II Low iodine	+898	+770	+1.17	+1.00
Thyroid-ecto-mized	III Adequate iodine	−73	−83	−0.131	−0.149
	IV Low iodine	−243	−251	−0.452	−0.467

*Changes in animals that died during course of experiment are included.

TABLE II.—INTAKE OF FOOD: RELATION TO CHANGES IN SURFACE AREA

Animals	Groups	Food intake for group, gm.		Gain or loss of surface area per gm. of food intake per 24 hrs.
		Total	Average per sq. cm. of surface area per 24 hrs.	
Intact	I Adequate iodine	13,162	0.0534	+0.061
	II Low iodine	13,313	0.0541	+0.058
Thyroid-ecto-mized	III Adequate iodine	5,762	0.0383	−0.014
	IV Low iodine	4,818	0.0327	−0.052

TABLE III.—INTAKE OF WATER: RELATION TO CHANGES IN SURFACE AREA

Animals	Groups	Intake of water			Gain or loss of surface area in sq. cm. per c.c. of water
		For group, c.c.		Ratio of, to intake of food*	
		Total	Average per sq. cm. of surface area per 24 hrs.		
Intact	I Adequate iodine	17,980	0.0701	1.3	+0.044
	II Low iodine	17,461	0.0680	1.3	+0.038
Thyroid-ecto-mized	III Adequate iodine	10,050	0.0652	1.7	−0.008
	IV Low iodine	11,424	0.0781	2.4	−0.022

*Ratio of cubic centimeters of water to grams of food.

TABLE IV.—CALORIC INTAKE AS FOOD, BASAL CALORIC OUTPUT (CALCULATED FROM OXYGEN CONSUMPTION) AND PERCENTAGE DEVIATION OF METABOLIC RATES FROM THOSE OF CONTROL GROUPS.

Animals	Groups	Average caloric intake or output per sq. m. per 24 hrs.		Basal metabolic rate, percentage deviation from normal caloric output	
		Intake	Output (basal metabolism)	Basis 1,032	Basis 588
Intact	I Adequate iodine	1,922.4	1,032	0	
	II Low iodine	1,947.6	1,090	+6	
Thyroidectomized	III Adequate iodine	1,378.8	588	−43	0
	IV Low iodine	1,177.0	482 (432)*	−53 (−58)*	−18 (−27)*

*One animal with regenerated thyroid tissue (rate −30) was excluded.

iodine intake consumed almost as much food as the controls receiving iodine, yet they lost more than three times as much weight and surface area. That is, the thyroidectomized animals that received iodine utilized their food better than the thyroidectomized animals which did not receive an iodine supplement.

A study of water intake in relation to surface area, to change in surface area and to the intake of food showed (Table III) that the water consumption in intact animals on either low or adequate iodine intake was not altered significantly. The water intake in thyroidectomized animals on low iodine intake, however, was significantly greater than in the thyroidectomized animals receiving iodine. This was evident in relation to surface area as well as to the food intake. For every gram of food taken by the thyroidectomized animals receiving supplemental iodine, 1.7 cubic centimeters of water was consumed, while the thyroidectomized group on low iodine consumed 2.4 cubic centimeters of water for each gram of food. The expression of loss of surface area in relation to water consumed indicates that the loss was approximately proportional to the loss calculated on a basis of food intake; that is, even though the water consumption was greater, the loss in weight and surface area

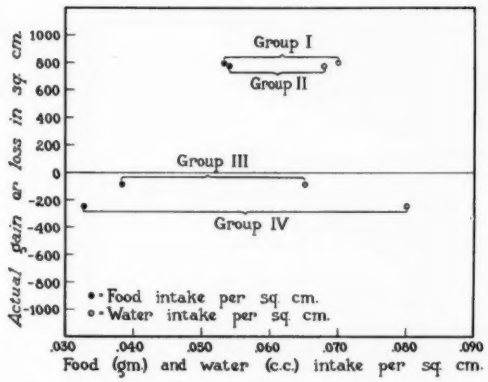

Fig. 2. Relation of intake of food and water to change in surface area. The length of the brackets indicates the ratios of food to water intake in the groups.

progressed. It is probable that the changes in weight and surface area were independent of the water intake and that the animal had diuresis and not retention of water. The relative differences in the amounts of food and water consumed and in the change in surface area of the 4 groups of animals are shown in Figure 2.

The metabolic rate of the animals was determined on the 49th and 64th days of the experimental period; a slight decrease in the oxygen consumption occurred in the second determination. The average of the two determinations was selected as a basis for comparison of the metabolic rates in the 4 groups (Table IV). A slight increase, 6 per cent, in the average basal metabolism of the intact (goitrous) animals receiving low amounts of iodine over that of the intact animals receiving adequate amounts of iodine may not be of sufficient magnitude to be significant. However, a real difference between the mean metabolic rate of the two thyroidectomized groups, with and without the iodine supplement, was observed. If the one animal in the thyroidectomized group which did not receive any iodine supplement and which showed regenerated thyroid tissue at necropsy was excluded, then the basal metabolic rate for this group was depressed 27 per cent below that of the thyroidectomized control group receiving the iodine supplement.

Caloric value of the food intake of the groups was calculated (Table IV). However, as this was not consumed under basal conditions the comparison with the caloric output is only relative.

EVALUATION OF STUDY

The presence of thyroid tissue in the intact animals permitted utilization of the small amount of iodine available in the low iodine diet. To accomplish this the thyroid hypertrophied, thereby maintaining the growth and well-being of the organism, as shown in the growth curve of the two intact animal groups.

The thyroidectomized animals, on the other hand, deprived of tissue especially adapted to the processing and utilizing of iodine, suffered a change in body growth and function. Unlike the intact animal groups, however, the presence or absence of a plentiful supply of iodine made a distinct difference in the performance of the thyroidless animals. This was evident in the depressed growth curve, the less efficient utilization of food, the greater intake of water and the distinctly lowered metabolic rate associated with the restricted iodine intake in the athyroid animal as compared with a similar group of animals receiving an iodine supplement. It is evident that iodine played some rôle in the body economy of the thyroidectomized animals.

The possibility that iodine may have an effect on vital processes in the absence of thyroid tissue was emphasized by the work of Swingle, Hoskins and Hoskins, Allen, and others who showed that iodine stimulated metamorphosis in thyroidectomized amphibians. Further evidence that iodine may affect growth processes in the absence of thyroid tissue was shown by Silberberg amd Silberberg, who reported stimulation of growth of bone in immature thyroidectomized guinea-pigs by the administration of iodine. This resulted in a parallel to the growth of bone caused by the administration of thyroxine to thyroidectomized animals.

Abelin, Ludwig and von Mutzenbecher, Salter and Lerman, Block, and others have demonstrated the production of thyroxine, diiodotyrosine and calorigenic protein similar to thyroglobulin by the iodization of organic material *in vitro*.

It is possible that iodine in the thyroidless animal acted in a similar manner to that of iodine on organic matter in vitro, possibly aided by enzyme action not necessarily confined to thyroid tissue. This effect of iodine in the thyroidless animal, then, may represent the action on the tissues of a certain concentration of iodine, thus elaborating a thyroxine-like substance.

If an extrathyroidal utilization of iodine exists, then its function in disease associated with iodine metabolism may be significant, especially in hypothyroid states. The untoward effects of iodine lack in the athyroid animal suggest that an absolute iodine deficiency would impose a more severe strain on the organism and that life itself may not be compatible with the complete absence of iodine.

SUMMARY AND CONCLUSIONS

A difference in iodine level in the diets of thyroidectomized rats significantly altered the changes in weight and surface area, the water intake, the food utilization, and the metabolic rate. These changes were not induced in the intact animals by deprivation or administration of iodine.

From the data presented it is concluded that iodine may play a rôle in body metabolism in the absence of thyroid tissue, possibly by the production of a thyroxine-like substance in the tissues.

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THE DIAGNOSIS AND TREATMENT OF CANCER OF THE STOMACH

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BECAUSE cancer of the stomach has received so much attention in recent years, further comment at this time would seem to be superfluous. Several extremely discouraging facts stand out so vividly, however, that one is justified in reviewing the present status of the problem as it is obvious that even greater efforts will have to be expended if any appreciable improvement is to be achieved in the early diagnosis and treatment of cancer of the stomach.

The seriousness of cancer of the stomach may be emphasized by comparison of the 5 year survival rates of all patients who have a malignant lesion in the more common sites, whether treatment has been given or not. With the possible exception of primary carcinoma of the lung, the 5 year survival rate after the diagnosis of cancer of the stomach is appreciably lower than the 5 year survival rate in cases in which a diagnosis of cancer of the fundus of the uterus (55 per cent), thyroid gland (42 per cent), breast (32 per cent), uterine cervix (31 per cent), or large intestine (24 per cent) has been made.

Walters, Priestley, and I have reported elsewhere the results of the study of a large group of cases of malignant lesions of the stomach. From a study of these cases, it was noted that of all cases in which a diagnosis of a malignant lesion of the stomach had been made, operation was performed in only 57.7 per cent (surgical rate) and that resection of some type was possible in only 25.8 per cent. The immediate hospital mortality in the group of cases in which resection was performed was 16 per cent, which, when translated into terms referring to the total number of patients observed, reduces the number of patients who theoretically have any chance of survival to 21 persons for each 100. In 28.9 per cent of cases in which a malignant lesion of the stomach was successfully treated by resection the patients were found to be alive at the end of 5 years, whereas only 6.2 per cent of the total number of patients observed with a malignant lesion of the stomach were alive at the end of the same period.

It is interesting to note the similarity in the operability rate and resectability rate in 127 cases of primary carcinoma of the lung reported by Overholt. In 41 per cent of the cases the lesions apparently were operable but in only 26 per cent of the cases exploratory operation disclosed the lesions were operable. At the time Overholt made the report, in 11 per cent of the cases in which the patients were living in which the malignant lesion had been removed, there was no evidence of metastatic involvement. It is impossible to determine at this date the 5 year survival rate as only 3 of 13 patients with no evidence of metastasis had been operated on more than 5 years before the report was made, and for this reason it is obvious that the 5 year "salvage" rate for the total number of patients observed will be appreciably less than 11 per cent and probably will be very close to that already mentioned for malignant lesions of the stomach.

The fact that early removal of a malignant lesion of the stomach is the only known method of cure has been emphasized repeatedly and is so widely accepted that repetition at this time seems trite and elementary. It may be assumed that because our study has been based on all cases of malignant lesions of the stomach observed in the years 1907 to 1938, inclusive, the surgical rate of 57.3 per cent and the resectability rate of 25.5 per cent will be low when compared to similar figures based on experience during the last 15 years. Unfortunately, such is not the case. The ratio of patients operated on to total patients who were found to have a malignant lesion of the stomach has varied

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little during the last 15 years from the surgical rate for the whole period and although the ratio of patients who underwent resection to the total number of patients is slightly higher than the rate of 25.5 per cent, the improvement is so insignificant as to be negligible.

The answer to this difficult and discouraging problem is not easy. One of the first responsibilities of the medical profession is to spread the knowledge that, with proper care, cancer of the stomach (in the broad sense) can be cured if it is attacked when the process is in its early stages and is localized in the stomach. That the symptoms of cancer of the stomach may be vague and ill defined is well known. Laymen must understand that there is no typical symptom complex that is characteristic of cancer of the stomach, and the physician and surgeon likewise must not wait for the development of characteristic symptoms before considering the possibility of the presence of a malignant lesion of the stomach and insisting upon a thorough examination in order to arrive at a correct diagnosis.

An attempt was made to classify the symptomatological picture presented by the patients who had cancer of the stomach in the group previously mentioned. This proved to be a difficult task because of the great variety of detailed symptomatological aspects inherent in such a large series of cases. The "unusual" type of symptomatological picture of a malignant lesion of the stomach occurred in three-fifths of the cases and consisted of a symptom complex in which dyspepsia was the most prominent symptom and was associated with varying degrees of decline. Thirty per cent of the patients portrayed the symptomatological picture of "ulcer," which was characterized by epigastric pain occurring characteristically when the stomach was empty and which was relieved by the ingestion of food or alkali. Seven hundred ninety-three patients who had a malignant lesion of the stomach had received some type of therapy for ulcers and 81 per cent of these patients had experienced definite subjective improvement. The observation would seem to discredit the value or the advisability of the use of the response to treatment as a criterion for distinguishing a malignant lesion from a benign ulcer except under the most nearly accurate conditions of observation, which it is possible to obtain.

A reason for the discouragingly low surgical rate in cases of malignant lesion of the stomach has been suggested by the supposed frequency with which such lesions manifest themselves at such an advanced stage of development that the lesion is inoperable before the patient experiences symptoms which suggest its presence. That this occurs occasionally is well known. That this occurs frequently is not substantiated by the fact that only 18 per cent of this large group of patients had noted the first symptom referable to the stomach less than 3 months prior to their admission to the clinic, whereas exactly half of the patients stated that they had experienced symptoms referable to the stomach for more than a year. It should be noted especially that the fact that a patient may have had symptoms referable to the stomach for a long time is no criterion upon which to exclude the presence of a malignant lesion of the stomach.

Among laymen, and particularly among physicians, there has been a lamentable lack of appreciation of the malignant potentiality of gastric ulcer. This statement does not suggest that all malignant lesions of the stomach start as benign ulcers. It is impossible from a pathological or clinical standpoint to determine how frequently this may occur, perhaps not over 10 per cent, perhaps never. It is not really so important to quibble as to whether or not a particular malignant lesion was once a benign ulcer as to attempt to determine immediately whether or not the lesion under consideration is malignant. Through bitter experience it has been learned that there is no method by which an unequivocal clinical diagnosis may be made as to the malignancy or benignancy of any ulcerating lesion of the stomach. In spite of the fact that the most outstanding advances in the diagnosis of cancer of the stomach can be attributed to roentgenology and gastroscopy, and that all other diagnostic methods in comparison become so insignificant that their importance can be disregarded, expert roentgenologists and gastroscopists admit that it is impossible in many instances to distinguish between a small ul-

cerating carcinoma, a malignant gastric ulcer, and a benign gastric ulcer. In our experience at the Mayo Clinic, approximately 9 per cent of carcinomatous ulcers had been diagnosed as benign by a roentgenologist, and what is even more significant, in 18 per cent of all cases of cancer of the stomach in which roentgenologic diagnosis was made, it was not possible to determine the exact nature of the lesion, and in 7 per cent of the cases a diagnosis of benign ulcer was made. It is particularly significant that some type of abnormal lesion of the stomach was noted in 99 per cent of cases in which a malignant lesion of the stomach was present. The fact that it is impossible to determine definitely by means of roentgenologic or gastroscopic examination the exact nature of certain lesions of the stomach is not surprising. This statement is not a criticism of either of these diagnostic methods. The two methods of examination of the stomach are supplementary and in many instances either one or the other may demonstrate an abnormal condition in the stomach while the remaining method may produce essentially negative results. A similar experience was recorded by Allen and Welch in a paper read before the American Surgical Association this year. This study dealt with 277 cases in which a surgical diagnosis of gastric ulcer was made. In 35, or 14 per cent, of the cases the lesion finally proved to be cancer. From this study, Allen and Welch have seen fit to recommend operation if: (1) the gastric ulcer is of short duration and the patient is more than 50 years old; (2) the ulcer is more than 2.5 centimeters in diameter; (3) there is no free hydrochloric acid in the gastric contents; (4) the ulcer is situated on the greater curvature or in the prepyloric region; (5) the ulcer is chronic and is on the lesser curvature. They recommend hospital observation and treatment for 1 month if: (1) the ulcer is acute and the patient is young; (2) the ulcer is less than 1 centimeter in diameter; (3) the ulcer is on the lesser curvature or on the anterior or posterior wall. If healing of the ulcer is complete in 1 month they said that repeated observation should be made 1 month after dismissal of the patient from the hospital. If healing is not complete in 1 month, as determined by roentgenologic and gastroscopic examination, then operation is advisable. My associates and I are in complete agreement with the principles of these conclusions. The fact cannot be emphasized too strongly however, that although the ulcer may give every evidence of having healed roentgenologically, gastroscopically, subjectively, and by the disappearance of occult blood from the stools, a malignant lesion may be demonstrated within a very few weeks after the fulfillment of these accepted criteria for a benign lesion.

TREATMENT

The purpose in treating cancer of the stomach is two-fold. The first is to effect a cure, if possible, and the second is to prolong life and reduce to a minimum the suffering which may be associated with the disease. It is obvious that the first purpose can be accomplished only by extirpation of the malignant mass together with accessible lymph nodes that are involved, including all of those in the greater omentum. In most instances, as shown by Carman, the question of operability, from the roentgenologic standpoint, depends on the situation, the extent, and the character of the cancer. He divided the stomach into 3 zones: the operable zone, corresponding to the pars pylorica; the borderline zone, corresponding to the pars media; and the inoperable zone, corresponding to the pars cardiaca. Tumors that are inoperable are usually situated in the cardiac end of the stomach, or have spread from a pyloric or fundic position to within the inoperable zone. Only rarely is a preoperative report of inoperability of a lesion in this situation not confirmed when exploratory operation is performed.

Roentgenologic evidence alone, however, should not be sufficient evidence in occasional cases to deny the patient what benefit may be derived from surgical exploration. This is particularly true of lesions situated primarily in the fundic portion of the stomach or near the cardiac orifice, as great strides have been made in the transpleural approach to these lesions. Although improvement in the "salvage" rate of patients with malignant lesions of the stomach may be expected with

the development and refinement of the more extensive surgical procedures, a more promising field undoubtedly exists in widespread promulgation of the importance of early diagnosis and recognition of the malignant potentiality of every ulcerating lesion of the stomach.

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USE OF FEMALE SEX HORMONES IN CLINICAL PRACTICE

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ENDOCRINOLOGY during the past decade has been a veritable handmaiden of gynecology. Despite a widespread and often uncritical organotherapeusis, which has not failed to draw repeated criticism from conservative clinicians, securely established indications have now been delineated for the use of the newer hormones in everyday practice. Equally, if not more important, contributions of endocrinology, however, have been manifest in the resultant evolution of a newer and more physiological approach to the handling of many of the ills of woman, which emphasizes diagnosis of functional levels and has as its desideratum the utmost salvage of function and the preservation or restoration of the fertile state when it is possible. There is now less recourse to function-destroying surgery and roentgenotherapy, unless it is founded upon securely established indications.

The ovary elaborates two kinds of "female sex" hormones: *estrogenic substances* (*estrogens*) from the granulosa cells of maturing graafian follicles and also from the cells of the corpus luteum and *progestational substances* (*progestin*) from the lutein cells of the corpus luteum. *Estrogens* are responsible for the manifold definitive changes in the sexual apparatus, and elsewhere, which characterize the adolescent epoch of sexual maturation and for the maintenance during the reproductive years of a state of development in the sexual organs compatible with the functional requirements placed upon them. These hormones are largely responsible, therefore, for the objective and subjective femininity of woman. *Progestin* is concerned with the preparation of the uterus in particular and the woman in general for the monthly physiological anticipation of pregnancy and, when gestation does occur, with important rôles in the nutrition and protective sheltering of the developing fetus. Opposing to some extent and, perhaps, also acting as synergists or pacemakers to these female sex hormones, are the contrasexual *androgenic* hormones which are elaborated in woman solely by the adrenal cortex. Woman's hormonal moiety must be viewed then as being dual in sexual nature: as Blair-Bell has observed, the older view that *propter ovarium solum, mulier est quod est* is less a real statement of fact than *propter secretiones internas totas, mulier est quod est.*

All of the ovarian and cortical adrenal hormones are steroids, or higher alcohols, which contain in common the cholane nucleus. Three different estrogenic hormones have been identified in woman's urine: estrone, estriol, and estradiol. Commercial preparations of all of these are available for therapeutic usage. These estrogenic hormones should be contrasted with certain nonhormonal drugs which possess estrogenic properties, but which have no chemical relationship to the natural steroids, for example diethylstilbestrol and its esters. During recent months diethylstilbestrol has been released into commerce by the Food and Drug Administration. Only one active progestational hormone, progestin, has been recovered in small amounts from woman's ovaries and urine. Another progesta-

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tional steroid, anhydro-oxyprogesterone, has been prepared synthetically from estradiol. Both of these progestational steroids are available commercially. While four 17-ketosteroids of adrenal origin have been recovered from woman's urine, androsterone, dehydroisoandrosterone, isoandrosterone, and etiocholanol3(α)-17-one, only two of these, androsterone and dehydroisoandrosterone, possess significant masculinizing or androgenic properties (2). Only the androgens, testosterone, which has been recovered from testes but not from urine, and its derivative, methyl testosterone, are used therapeutically.

USES OF ESTROGENS

Consideration of the known pharmacological properties of estrogens has justified as rational their trial under the following circumstances (9): (1) in certain established instances of estrogenic ovarian failure, occurring in adolescence or during sexual maturity, as substitutional or complemental therapy; (2) in certain subjective disturbances of the climacteric as palliative but not full substitutional therapy; (3) in hypomastia for cosmetic effects alone; (4) in certain hyperfunctional states of other glands, i.e., the pituitary or adrenals, as antagonistic therapy; and (5) in certain cases for specific pharmacological effects upon the vaginal epithelium, the indication for therapy not being any endocrine disturbances.

In addition to these apparently rational indications, estrogens have been employed empirically and often contraphysiologically under various conditions.

Substitutional therapy in intrinsic ovarian failure. When severe grades of estrogenic failure of this character exist, the indication for therapy concerns the completion of sexual maturation in the adolescent and the prevention or correction of sexual regressions in the adult. Large doses of estrogens will produce dramatic endocrine responses under these circumstances, for the endocrine function of the ovaries can be substituted for just as effectively as that of the pancreas or the thyroid. Three important facts limit the practicality of prolonged substitution at the ovarian level: (1) the expense involved: the large dosages of estrogens required day after day and year after year have imposed in the past an almost insurmountable financial burden, but the commercial availability of diethylstilbestrol has now circumvented this limitation; (2) the inability to overcome the sterility of the patient: the germinal function of ovaries cannot be substituted for; and (3) the temporary nature of the results obtained: regressions which erase, for the most part, all therapeutic results, occur when treatments are discontinued.

Fortunately, in view of these limitations, severe estrogenic deficiency rarely impairs health or somatic efficiency despite the cosmetic inelegancies it may impose upon the adolescent or the young woman. A limited trial of substitutional therapy is justified in the young woman with severe estrogenic deficiency upon the following grounds: (1) to attempt to curb the abnormal somatic overgrowth of these young patients by effecting epiphyseal closures, a therapeutic hope not definitely established as a fact; (2) to bring about some degree of sexual attractiveness of the patient, for its salutary psychic effects; and (3) to alter beneficially the ovariopituitary reciprocities of these patients by the resulting genital growth and development (9).

Complemental therapy in intrinsic ovarian failure. Intercurrent episodes of intrinsic ovarian failure occur, as for example, the occasional sterile (anovulatory) cycles which even normal, healthy women may have. A preponderance of these may produce sterility and eventual distressful menstrual irregularities.

Frequently excessive or prolonged uterine bleeding of the young woman is due to these intercurrent episodes of lowered receptivity of the ovaries to gonadotropic influences from the pituitary. The employment of a system of cyclic steroid therapy embracing the use of estrogens and progesterone under these circumstances permits effective control of the uterine bleeding without any further damage to ovarian function; in fact, not infrequently, this therapy may permit tiding the patient over this ovarian crisis until such time when normal function returns (11). Without such supportive therapy, doubtless many of these

intercurrent episodes progress to graver degrees of ovarian failure.

These statements regarding the effectiveness of the hemorrhagenic-hemostatic schedule permitted by cyclic steroid therapy should not be construed as representing the advocacy of endocrine therapy solely to regulate the menstrual cycle. Many menstrual irregularities are innocuous, if not actually fanciful, and endocrine therapy under these circumstances is meddlesome and often contraphysiological.

Palliative therapy in the physiological estrogenic failure of the climacteric. It is trite to state that estrogenic deficiency is physiological at the time of the climacteric, yet, some of the massive doses of estrogens given at this time of life by some organotherapeutic enthusiasts would indicate apparent ignorance of the normal hormonology of this epoch. No need seems to exist for prolonged therapy with full substitutional or even larger dosages of estrogens at the time of the climacteric. Our knowledge of geriatrics has not reached such a state that we are justified in trying to postpone sexual aging.

All estrogenic therapy during the climacteric should fulfill this general therapeutic desideratum: to lessen, but not to substitute for, the physiological ovarian deficit of those women in whom severe subjective symptoms characterize this epoch, i.e., palliative, not full replacement therapy. Therapy should be limited if possible in duration to several months; dosages should be kept small and estrogens should be given orally if possible. If patients to be treated continue to have episodes of bleeding, therapy should be adjusted cyclically so that it is withdrawn at the time of and during episodes of bleeding, lest troublesome menstrual irregularities be added to the other symptoms of the patients.

Cosmetic therapy of hypomastia. A general statement regarding isolated hypoplasias of the genital system seems advisable at this time. When a woman, who is apparently endocrinally adequate otherwise, has unilateral or bilateral hypomastia or a hypoplastic uterus, the likely diagnosis is a faulty end-organ or end-organs rather than faulty ovarian function. Estrogenic therapy under these circumstances is usually of no benefit.

At times a patient with typical adolescent hypo-ovarianism is concerned solely by her hypomastia. The use of estrogenic ointments by local massage applied to the breasts may give gratifying temporary results if rather large doses of estrogens are employed and some permanent benefits may result, probably due chiefly to massage. It has been reported that the concomitant use of progesterone by injection lessens the regressions which follow the discontinuation of estrogens.

Antagonistic therapy of hyperfunctional states of other glands. Theoretical considerations have suggested that large doses of estrogens given over prolonged periods may offer a means of depressing hyperfunctional states of the pituitary and of nullifying the virilizing effects of hyperactivity of the androgenic elements of the adrenal cortex. The results of estrogenic therapy in neither of these conditions have been satisfactory despite the fact that it seems well established that the moderate gonadotropic hyperactivity of the pituitary which characterizes the climacteric is reduced by adequate estrogenic therapy. Larger dosage and more prolonged usage of estrogens permitted by recently available diethylstilbestrol may have better results

Therapy for local vaginal effects. The special trophic effects of estrogens upon the vaginal epithelium have permitted effective applications in the treatment of gonorrheal vaginitis of childhood and of nonspecific postmenopausal vaginitis. Since hypoestrogenism is physiological at these two periods of life, estrogens do not fulfill the requirements of hormonal agents but rather of active substances having a desired local action: the production of vaginal cornification and increased vaginal acidity, both of which effects augment the resistance of the host to the invading organisms. Since estrogens are active when applied directly to the vagina, and since large doses are not required, undesired general effects of this therapy (precocious adolescent phenomena and uterine enlargement with return of uterine bleeding, respectively for the two classes of patients) may be avoided.

Good results have been reported by some gynecologists from the local use of estrogens before operation in postmenopausal women

awaiting plastic vaginal procedures. The modus operandi of this therapy is similar to that in vaginitis. The improvement in vaginal proliferation has been said to facilitate operation and postoperative healing.

Empirical and contraphysiological therapy. Time does not permit even a listing of the various empirical and contraphysiological uses to which estrogens have been put. Most of these have been concerned with the treatment of subjective symptoms, by fact or theory, usually the latter, related to disordered ovarian function.

An explanation is due, perhaps, in regard to our meaning of contraphysiological therapy. When estrogens are used in large doses in women with apparently normal ovarian function with the hope that ovulation and corpus luteum function can be prevented, which has been stated to be the rationale of such therapy in dysmenorrhea and "menstrual migraine," this in our opinion constitutes contraphysiological therapy.

Recently another type of contraphysiological therapy has been reported. Dunn has given male criminals with abnormal sexual histories large doses of diethylstilbestrol for the purpose of depressing the endocrine function of their testes. He was apparently quite successful and, in addition, observed markedly degenerative changes in their seminal tubules.

USES OF PROGESTERONE

All of the therapeutic applications of progestin (progesterone) and anhydro-oxyprogesterone have been concerned with the substitution for or the complementation of corpus luteum failure during the progestational phase of the menstrual cycle or during pregnancy. In the first category, the following conditions come up for discussion: dysmenorrhea, estrogenic bleeding, and ovarian sterility; in the second instance, repeated or threatened abortions.

Dysmenorrhea. In line with the widely accepted theory that the corpus luteum exerts a quieting effect upon uterine motility, it seemed logical to employ progesterone, when it became available commercially, in the treatment of functional dysmenorrhea. Since results that followed were no better than those obtained from diverse other therapeutic agents, it seemed logical to question the occurrence of any specific action. The reason for this therapeutic failure of progesterone seems obvious. Most women with functional dysmenorrhea have no evidence of corpus luteum deficiency, i.e., they bleed from progestational endometria and excrete essentially normal amounts of pregnandiol (a metabolic product of progestin) (6).

Estrogenic bleeding and ovarian sterility. Most of the functional disturbances of menstruation are characterized by estrogenic (anovulatory) bleeding and an associated sterility, i.e., lack of corpus luteum function. It seemed rational to use progesterone in the treatment of these conditions.

Misconceptions occurred at first in regard to the pharmacological effects to be expected from progesterone. It was believed that injections of progesterone would postpone bleeding (i.e., lengthen the interval) when given during nonbleeding phases and that, when given during episodes of excessive bleeding, progesterone would have a hemostatic action. In 1936, we (5) called attention to the fact that the exact contrary was true: progesterone has a hemorrhagenic effect when given during nonbleeding phases and increases the amount of bleeding when given during flowing.

Another error in therapeutic theorization was the assumption that a "medical curettage" in these cases, especially in patients with excessively proliferated endometria, could be produced by progesterone by transforming the endometrium to a full blown progestational one which in turn would be shed in the normal fashion. As early as 1936 (5) we cited the infrequent occurrence of progestational responses in these patients following progesterone therapy even when progesterone was synergized with ample estrogens. This phenomenon was related by us to some factor which brought about a lowered endometrial reactivity to progesterone (11).

In regard to the sterility associated with estrogenic bleeding, it seems unlikely that even effective substitution for the absence of progestin would induce ovulation any more readily than in the instances of adolescent ovarian failure wherein substitutional therapy

with estrogens is given. However, when estrogens and progesterone are given cyclically as in our regimen of cyclic steroid therapy until normal endometrial reactivity returns, a good number of patients experience a return of the fertile state.

Repeated or threatened abortion. Deficient function of the corpus luteum has been predicated to be the etiological factor in the recurrent or threatening abortions of women in whom no obvious organic or metabolic causes for these abortions exist. Progesterone therapy under these circumstances is founded upon the assumption that these patients need more of the uterine quieting effect of that hormone. Many reports have appeared dealing with the good results obtained from repeated injections of relatively small amounts of progesterone in patients with histories of having had numerous previous abortions.

We have cast doubt recently (8, 10) upon the correctness of the premise that corpus luteum deficiency is the cause of the abortions which are prevented presumably when progesterone is administered. Every patient of ours who had critically low pregnandiol (a metabolic product of progestin) excretions aborted despite intensive therapy with progesterone in amounts many times those commonly used. It is our belief that, if progesterone has a specific action in preventing abortions, its modus operandi is something other than that of complementing corpus luteum deficits.

USE OF ANDROGENS

Androgens are not considered usually to be "female sex" hormones but a brief discussion of these in this paper seems advisable. It is justified upon two grounds: (1) the fact that these hormones form a part of the normal hormonal pattern of woman; and (2) the fact that during recent years there has been a widespread use of androgens in gynecic therapy.

No clear-cut rationale has been established for the therapeutic use of these steroids in woman (7). The only justification for their use has been apparently that they have pharmacological reactions which under certain circumstances appear to be expeditious, i.e., suppression of ovulation, hemostasis in menorrhagia, pituitary stabilization in the climacteric without endometrial stimulation, suppression of lactation, etc.

All of the described effects of androgens have been due to the "negation" or "overriding" of the usual ovarian function, i.e., are contraphysiological effects (4, 12). Few, if any, of the ultimate results obtained by androgens cannot be accomplished more satisfactorily from measures less likely to cause undesired side effects. The use of androgens in the female is beset with the dangers of grave symptoms of virilization, not all of which are reversed when therapy is discontinued. One theoretical indication for androgenic therapy is to antagonize hyperestrogenism. The only true and proved instance of this which we know clinically is that which is due to granulosa cell tumors of the ovaries, for which the recognized and satisfactory treatment is surgical ablation of the tumor.

SUMMARY

Estrogenic hormones have a limited, but well established, rôle in the treatment of certain climacteric syndromes, gonorrheal vaginitis of childhood, and senile vaginitis. Complemental therapy with estrogens and progesterone in certain instances of intercurrent ovarian failure may be followed by the return of normal ovarian function. Substitutional therapy in severe estrogenic failure of the adolescent or young woman yields only temporary results and does not circumvent the sterility of these patients. Untoward responses to estrogenic therapy are increasing since the availability of cheap, orally active estrogens of the diethylstilbestrol type; these are due chiefly to overdosage. Diligence to avoid overtreatment should be observed.

Despite the expectations aroused by the commercial availability of progesterone, no definitely established therapeutic rôle has been accorded it. As a part of cyclic steroid complemental therapy in estrogenic bleeding, it has given best account of itself. Its specific value in dysmenorrhea and repeated or threatened abortion is questioned.

Androgens have no place in rational gynecologic therapy. Their effects are solely of ovarian negating or depressing type. Viriliz-

ing effects from the use of androgens do not always disappear when the treatments are discontinued.

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VISUAL FIELD CHANGES AND SUBDURAL HEMATOMAS

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IT is universally agreed that the clinical diagnosis of subdural hematoma is extremely difficult. Many authorities stress the importance of making exploratory burr holes when the diagnosis is in doubt. A negative burr hole is much less serious than a neglected subdural hematoma. In an effort to improve our diagnostic acumen in respect to this condition we have recently reviewed the series of verified subdural hematomas seen on the neurosurgical service of the Cincinnati General Hospital since October, 1937. In the course of this review we were surprised to find that in slightly more than 10 per cent of the cases some mention of a visual field defect was recorded. Knowing the difficulty in examining visual fields, even roughly, in unco-operative patients this percentage seemed remarkable. It, therefore, seemed probable that a brief review of the type of visual defect, the diagnostic and prognostic value of such defects, and the underlying pathological changes behind the defects might be worthy of brief consideration.

In a series of 62 verified subdural hematomas there were 7 instances in which visual field defects were mentioned (Table 1). In 4 instances these were apparently a very definite finding borne out by careful confrontation tests. In 3 instances the defect was said to be probable. In 1 of the 4 definite examples it was possible to check the fields by actual careful perimetry. In all the cases the defect was homonymous in character. The homonymous defect was contralateral to the hematoma in 4 instances; in 1 case the clot was centrally placed, that is interhemispheral, and the defect was a left homonymous abnormality, and in the seventh case the visual field change was ipsolateral. Five of the patients recovered and were discharged from the hospital. In 4 of these postoperative checks of the visual fields revealed no definite abnormalities. In the fifth case that recovered the preoperative homonymous defect had been very definite. A postoperative check 2 weeks after surgery showed a residual, almost complete left homonymous defect. This was checked again 1 month after the operative procedure, and there was definite evidence of recovery. A third perimetric study was done approximately 2 months after the removal of the subdural hematoma, and at this time the fields continued to show improvement (Fig. 1).

Pathological studies were carried out on the brains of the 2 patients who died. In both cases there was definite evidence of herniation of the uncal portion of the hippocampal gyrus. In both, the greater herniation was in the right side. The clinical evidence in each instance had pointed to a left homonymous visual field defect. In the examination of both brains there was a suggestion that circulation in the posterior cerebral artery on the right had been interfered with by the uncal herniation. The first fatal case (No. 4) was the one in which the hematoma had been interhemispheral. There was gross evidence of moderate softening in the distribution of the right posterior cerebral artery. However, in the second case (No. 7) there was very definite gross and microscopic evidence of bilateral posterior cerebral artery involvement with encephalomalacia. This change was much more extensive on the right, the side on which the

TABLE I.—SUMMARY OF CASES REPORTED WITH EMPHASIS ON VISUAL FIELD AND PUPILLARY CHANGES

No.	Side of clot	Visual field change	Pupillary change	Mortality
1	Left	Right homonymous	Right>Left	Relieved
2	Right	Left homonymous	Right>Left	Relieved
3	Left	Right homonymous	Left >Right	Relieved
4	Central	Left homonymous	Left >Right	Died
5	Right	Left homonymous	Right>Left	Relieved
6	Left	Left homonymous	Right>Left	Relieved
7	Right	Left homonymous	Right>Left	Died

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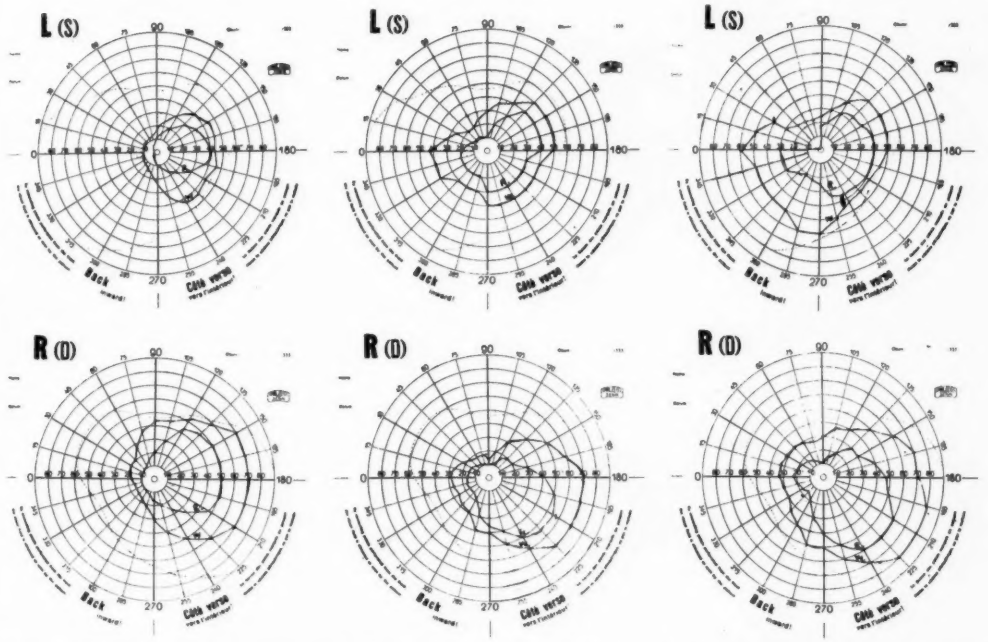

Fig. 1. Shows progressive improvement in left homonymous hemianopia 2 weeks, 1, and 2 months after removal of a right subdural hematoma. Because of poor co-operation the fields are not entirely congruous.

hematoma had been found at operation. In neither case was there evidence of actual thrombosis or complete occlusion of the posterior cerebral arteries.

The mechanism of the tentorial pressure cone or uncal herniation is no new concept. The manner in which this change may produce various types of false localizing signs has been discussed by Jefferson, by Kernohan and Woltman, and by Moore and Stern. More recently Schwarz and Rosner as well as Allison and Morison have published complete reviews of the pathological mechanism of embarrassment of circulation in the posterior cerebral artery with tentorial herniation. Reid and Cone were able to produce experimentally certain parts of the tentorial pressure cone syndrome, more particularly the pupillary changes. However, it is interesting to note in reviewing the cases reported by these various authors that none mentioned uncal herniation accompanying subdural hematomas. It also would appear that little has been written about the reversibility of the changes that may occur.

We believe that the visual field changes found in this series of subdural hematomas were most probably caused by embarrassment of the circulation in the posterior cerebral artery. Pressure from a herniated hippocampal uncus brought about slowing of the circulation and resulting anoxia in the occipital distribution of the posterior cerebral artery. It is fair to postulate that this change may be of any degree ranging from slight anoxia with transient functional impairment, through anoxia of such severe degree as to cause permanent functional impairment based on profound structural change, a mechanism discussed by Evans and McEachern. This supposition seems to fit the clinical and pathological facts found in this group of cases. It seems probable that in the patients that survived without residuals the factors causing the homonymous defect were mild and reversible. The patient who was followed for 2 months but still showed

slight visual field defects represented more severe tissue damage. Finally, the cases which came to postmortem examination represented examples of gross irreversible cerebral softening.

SUMMARY AND CONCLUSIONS

In reviewing a series of 62 subdural hematomas, 7 cases, 11 per cent, were found to show evidence of visual field defect.

The visual field defect was always homonymous in character. In 5 instances it was contralateral to the clot, one was ipsolateral, and in one the field defect was leftsided, the subdural clot being centrally placed.

Four patients showed complete recovery without residual visual field defects. In one patient careful checks of the fields were carried out at intervals and gradual improvement was observed.

It is believed that too little stress has been put on the complications caused by uncal herniation in cases of subdural hematoma. Moreover, it is felt that the visual field changes discussed in this report were caused by tentorial herniation and embarrassment of the circulation through the posterior cerebral artery. There seems to be good evidence that these changes may frequently be reversible.

Efforts should always be made to determine the presence or absence of visual field defects in patients suspected of having subdural hematomas. In this small series the visual field changes were twice as reliable as pupillary changes in attempting to laterlize the subdural clot. Like other clinical signs that may indicate uncal herniation, visual field changes should emphasize the importance of immediate surgical intervention in order to remove the cause of the herniation. The demonstration herewith of the apparent reversibility of the process emphasizes the importance of early effective removal of the source of the herniation.

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THE PROTECTION OF THE OPERATIVE FIELD WITH AN IMPERMEABLE ADHESIVE SKIN COATING

A Preliminary Report

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ANTISEPSIS in surgery is usually considered to have had its origin with Lister's presentation of carbolic acid as a combatant against postoperative infections. In one of his earliest communications he stated: "when it had been shown by the researches of Pasteur that the septic property of the atmosphere depended . . . on minute organisms suspended in it . . . it occurred to me that decomposition in the injured part might be avoided . . . by applying as a dressing some material capable of destroying the life of the floating particles." (18) Using his antiseptic methods in his wards at Glasgow, during the 3 year period ending in 1870, Lister succeeded in reducing the mortality rate in amputations from 45.7 per cent to 15 per cent (19). Since Lister's epochal contribution, asepsis in surgery has become a constant and eagerly sought desideratum. It is now generally realized that infection at operations may arise from several possible sources of contamination: (1) upper respiratory tract, hands, hair, skin, and clothing of the operating personnel, and all individuals entering the operating room; (2) the air of the operating room; (3) the instruments and paraphernalia employed in the operation; and (4) the skin of the patient.

Various attempts have been made to control these sources of contamination, the efficacy of which is dependent to a great extent upon the degree of exactitude in application. In 1928, Sutton quoted the statistics of several authors in which the percentages of postoperative infections ranged from 28 per cent to 6 per cent. A review of more recent articles reveals a decrease in the percentages of infection after clean surgical operations, with an average of approximately 3 to 5 per cent (4, 7, 9, 10, 13–15, 26, 27). Beck, in 1936, stated that the incidence of serious infections in clean surgical wounds has been lowered to 1 per cent and of trivial infections to 5.4 per cent. Of the previously mentioned sources of infection which may be present at operation perhaps the most difficult to control with absolute assurance is the skin of the patient. Hirschfeld stated that the normal skin rarely harbors fewer than 10,000 organisms per square centimeter. The general opinion prevails that no antiseptic yet introduced nor technique yet devised completely sterilizes the skin. "Of the many sources of wound infection, all, with the single exception of the skin of the operative field, are under the control of the surgeon if he operates with competent help and in proper surroundings" (39). This is clearly demonstrated by the numerous attempts to develop a method which will produce relative sterilization of the skin of the operative field. Even a cursory perusal of the literature will reveal numerous compounds and solutions which have been offered as antiseptics (1, 2, 5, 6, 10, 13, 17, 21–42). A random selection of reported incidences of sterility following the use of four widely employed antiseptics are as follows: merthiolate, 95.4 per cent; tincture of iodine, 71.7 per cent; mercurochrome, 34 per cent; metaphen 91.1 per cent; and several others grouped together, 65 per cent (5, 16, 24, 28, 34, 36, 38, 41, 42). Each antiseptic has its advocates who make glowing claims for its value and its opponents who caution against its uncritical use or condemn it entirely. Allen and associates ob-

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served that the morbidity rates are not widely divergent even though there are clinical differences between the various antiseptics. Hirschfeld stated that in spite of the different preoperative preparations, the incidence of wound infection in different clinics varies slightly. Almost as numerous as the antiseptics themselves are the various *in vitro* and *in vivo* experimental tests which have been performed to evaluate the effectiveness of these substances (5, 8, 13, 21, 22, 24, 28–30, 32, 33, 36, 38, 40, 41). It is fairly well agreed that antiseptics showing excellent *in vitro* tests may not be at all satisfactory in actual clinical use. Likewise, *in vivo* laboratory ratings may not give an accurate index of the quality of the antiseptic, for as Bass points out, organisms added to the skin are more easily killed than the "basic flora."

Price (31) has shown that there are two types of bacterial flora on the skin: (1) the *transient* flora which is loosely attached and can be removed in a few minutes of scrubbing; and (2) the *resident* flora which is tightly attached and is difficult to remove. In certain cases the resident flora may include virulent organisms as a result of prolonged exposure to their source. In addition, the bacteria of the deeper layer of the skin are brought to the surface by perspiration, especially during a lengthy operation, and may contaminate the wound because the antiseptic applied at the beginning of operation is no longer effective. Therefore, this source of contamination is a constant hazard whose threat increases commensurably with the length of the operation. Since the bacteria cannot be completely removed from the skin during the operation, their introduction into the wound may be prevented by sealing the operative field with a sterile impermeable surface. Such a surface film has been produced by the use of mercuric bichloride but unfortunately, due to perspiration, multiplication of bacteria occurs at an increased rate beneath the film (32, 33). Consequently, any injury to the film allows the escape of the bacteria into the wound.

The current method of preparing the operative field consists of shaving, careful soap and water scrub, defatting, application of an antiseptic agent, and draping of the area with sterile towels. After the incision is made, sterile towels are clamped to the edges to protect the wound from possible skin contamination. It is generally realized, however, that this careful preparation of the skin and the clamping of towels around the wound edges, are measures of only relative efficiency and that they do not absolutely protect the wound from such contamination.

Obviously, if there could be applied to the skin in the region in which the incision is to be made some impermeable substance which is sterile and which would adhere to the skin, the incision could be made through it and absolute protection from skin contamination would be afforded. Such a covering which would be most efficient should possess the following properties: (1) impermeability to bacteria; (2) bactericidal action; (3) nonirritancy; (4) transparency; (5) adhesiveness to skin; (6) elasticity; and (7) facile incisability.

Because it fulfilled all these conditions except the first three, "vinylite resin"[1] was tested for the possibility of fulfilling the other requirements. This resin is a polymerized vinylite acetate, which is soluble in practically all common solvents with the exception of water, gasoline, and the higher alcohols. It is colorless, odorless, nontoxic, and it resists dilute salt, acid, and alkali solutions. It is widely used as an adhesive for a variety of materials and is an excellent adherent to practically all types of surfaces. It absorbs water and becomes leathery and pliable when large amounts are absorbed (43).

Several preliminary tests were tried in the laboratory before clinical application was begun. Solutions of the resin were made in different percentages to determine the formula which gave a satisfactory coating and which dried most rapidly. On the basis of these studies, the following formula was adopted:

25 grams vinylite resin, AYAF
100 c.c. acetone
1.32 grams nitrocellulose (to hasten drying)

This solution of vinylite resin was applied to the skin of volunteers and allowed to remain intact from 24 hours to over a week. Its

[1]This material was supplied through the courtesy of Dr. A. G. Cranch, of the Carbide and Carbon Chemicals Corporation.

adhesiveness was definitely demonstrated and on peeling off the transparent resin, the skin beneath was dry and unaffected even at the end of a week. Skin irritation was never observed. Fifteen sterility tests were made. One-half cubic centimeter of resin was inoculated into tubes of meat digest broth and incubated aerobically and anaerobically for 4 days at 37 degrees C. At the end of this period, none of the tubes was sufficiently cloudy to justify the notation of positive. Therefore, all tubes were streaked on blood agar plates and incubated aerobically and anaerobically for 24 hours at 37 degrees C. Of the 30 plates, only one showed a growth of nonhemolytic Staphylococcus albus. An attempt was made to determine the bactericidal power of the solvent, acetone. Increasing dilutions of acetone were made with sterile broth, and these tubes were inoculated separately with staphylococcus, streptococcus, and Bacillus coli. At the end of 24 hours incubation at 37 degrees C., the tubes were replated and failed to show growth on the 1:1 dilution. Dilutions of 1:5 or higher had little or no bacteriostatic effect. Tubes of the prepared resin were inoculated separately with the same 3 organisms and transplants were made to tubes of meat digest broth and blood agar plates at the end of 8 minutes, 15 minutes, and 30 minutes. All tubes were negative and only one colony of staphylococcus grew on the plate made at the end of the 8 minute period.

Since the real test of the compound is its usefulness clinically, the vinylite resin solution was tried on a series of cases. For this purpose, 1 per cent phenol was added to the formula to enhance its bactericidal powers. It was determined that this produced no changes in the chemical and physical properties of the resin as described above. This vinylite resin solution was used in 30 clean surgical cases. The usual ward preoperative preparation of shaving and soap and water scrub was performed. In the operating room, the area was scrubbed with ether, and painted with vinylite resin by means of a soft rubber applicator, and draped with sterile sheets to limit the operative field. When the sterile drapes were thus applied over the vinylite resin before drying had occurred the sheets would adhere closely to the skin at the borders of the operative field and towel clamps for the purpose of holding the sheets in place are obviated. This is particularly advantageous in areas having curved and irregular surfaces, such as in breast or thyroid operations. When the solution was applied in proper thinness, drying was complete within 5 minutes. The length of time and the type of each operation were noted. Most of the operations consisted of appendectomies, thyroidectomies, cholecystectomies, herniorrhaphies, and phrenemphraxes, and the duration of the procedures averaged 46 minutes. In each case, 6 groups of bacteriologic studies, depending upon the site of swab cultures, were made as follows: (1) solution of vinylite resin; (2) the skin of the operative field immediately after the patient's entrance into the operating room; (3) skin surface after ether scrub; (4) skin edge after incision; (5) skin edge immediately before closure of incision; and (6) skin surface approximately 3 inches from the wound after the resin was stripped back and before the application of the dressings. The cultures were sent to the laboratory where each was streaked out on two blood agar plates and inoculated into two tubes of meat digest broth; one of each was incubated anaerobically and the other aerobically for 48 hours. At the end of this period, the plates were examined for growth, and the tubes were replated and incubated aerobically and anaerobically for a period of 24 hours.

The results of these bacteriological studies may be briefly summarized as follows:

Group 1. In 27 cases, the bacteriological studies on the solution of vinylite resin immediately before its application to the operative field showed no growth.

Group 2. In 30 cases the bacteriological studies made on the skin of the operative field before it was prepared except by shaving and washing with soap and water showed 100 per cent growth. Staphylococcus was recovered most frequently, which is comparable to other reports (11, 12, 14, 15, 26).

Group 3. In 30 cases, these studies on the skin of the operative field immediately after it was prepared by ether scrub showed the presence of growth in 11 (36.6 per cent) cases.

Graph 1. Graphic representation of incidence of positive growth in bacteriological studies on the use of vinylite resin.

Group 4. In 30 cases, the bacteriological studies of the skin edge immediately after the skin incision was made showed the presence of organisms in 5 cases or 16.6 per cent. Of these 5 cases, 4 were positive in group 3 and showed organisms with similar bacteriological properties.

Group 5. In 30 cases, these studies made on the skin edge at the completion of the operation and before the skin edges were closed showed the presence of organisms in 8 cases, or 26.6 per cent. Of these 8 cases, only 1 was also positive in groups 3 and 4, and 3 were also positive in group 3 alone.

Group 6. In 28 cases, bacteriological studies made immediately after the completion of the operation on the skin surface in the operative field under the vinylite resin showed the presence of organisms in 3 cases or 10.7 per cent.

EVALUATION

Whereas it is recognized that the results of these bacteriological studies are based upon too few cases to be of conclusive significance, they were considered of sufficient interest to be presented as a preliminary report. Moreover, it should be realized that these bacteriological studies were done with the purpose of determining whether vinylite resin solution would fulfill the desiderata previously considered in the ideal preparation of the skin of the operative field. The clinical application of this method of skin preparation clearly demonstrated that it fulfilled the requirements of transparency, adhesiveness to the skin, elasticity, ready incisability, and non-irritancy. The significance of these requisites of such a skin preparation is clearly apparent. Transparency is desirable because it permits the surgeon to place the incision accurately according to the landmarks which may be clearly seen. The significance of adhesiveness to the skin lies in the fact that unless the impermeable film adheres closely and tenaciously to the skin, there is the possibility that during the operative procedure perspiration containing organisms which have escaped from skin pores may readily seep beneath the film toward the edge of the incision. This is likely to be enhanced further by retraction and manipulation during the operative procedure. For this reason, the film must possess an elastic quality somewhat comparable to the skin to which it adheres. It was found that the vinylite resin film was readily elastic and simultaneously stretched with the skin and remained definitely adherent to it as the wound was retracted and manipulated. In fact it was observed that this adhesive and elastic quality remained present for several days after the operation. Moreover, skin irritation was never observed in any of the cases even after the film had been allowed to remain in contact with the skin for as long as one week. In a few cases the vinylite resin solution was applied to the irritated skin surrounding an enterostomy opening and it was found to have a definitely protective and beneficial effect. Obviously this is another purpose for which it may be used to great advantage.

The results of the bacteriological studies clearly demonstrated its bactericidal activity. Bacterial growth was obtained in none of the 27 cases in which these studies were made on the solution itself (Graph 1). This is particularly significant in view of the fact that no special attempt was made to sterilize the solution. Moreover, the solution was readily exposed to contamination since the rubber applicator was repeatedly dipped into the solution after it had been applied to the skin of consecutive patients.

The fact that bacteriological growth was obtained from the skin of the operative field in all of the cases after it had been prepared by shaving and washing with soap and water is to be expected and conforms with similar

previous studies (8, 22, 24, 31). It merely emphasizes further the importance of careful and more effective methods of preparing the skin of the operative field. Of particular interest is the fact that bacterial growth was obtained from the skin after ether scrub in 36.6 per cent. This would seem to indicate that ether has a sterilizing ability of over 60 per cent, but this is not in accord with other studies (20, 32, 34, 36). Price (32) has expressed the opinion that ether is valueless as a sterilizing agent of the skin. However, its detergent qualities are generally recognized and for this reason it is considered of definite value in the preparation of the operative field. Perhaps the unusually low incidence of bacterial growth after ether scrub in this series may be explained by the fact that this was performed with especial vigor and thorough care, 8 or 9 separate scrubbings being used. In our opinion this is significant and demonstrates the value of such careful mechanical cleansing.

The results of the bacteriological studies of the skin incision edges immediately after the incision was made and following the completion of the operation immediately before the incision was closed are also of interest. The fact that bacterial growth was obtained in only 16.6 per cent of the cases in the former instance and that this incidence had risen only 10 per cent in the latter would seem to indicate the effectiveness of this method of preparation. Somewhat comparable studies were made by Maddock and Georg (22), who found an average incidence of contamination (with the use of mercresin, merthiolate, and 2 per cent iodine-and-50 per cent propanol) of 37 per cent at the beginning of the operation and 60 per cent at the end of the operation, an increase of 23 per cent. Certainly if consideration is given other factors which may act as sources of contamination in increasing this incidence such as the air of the operating room and the manipulation of the wound with consequent squeezing out of bacteria at the skin edges the possibility that the skin of the operative field as a source of contamination in increasing this incidence would seem to have been reduced considerably. This would indicate further that the vinylite resin film is effective as regards impermeability. This is also supported by the fact that all of the wounds healed by primary union and in none was there any evidence of even trivial infection.

Perhaps one of the most significant findings in this connection is the fact that at the completion of the operation, bacterial growth was obtained from the skin of the operative field after peeling off the vinylite resin film in only 10.7 per cent of the cases. It must be admitted that this was an unexpected observation. Certainly if bacterial growth was obtained from this skin in 36.6 per cent of the cases before the film was applied, one would expect a higher incidence three-quarters of an hour later during which the factors of perspiration and manipulation of the skin with consequent escape of organisms may have been operative. The explanation for this unexpected decrease in bacterial growth probably lies in the observation that the skin was absolutely dry when the vinylite resin film was peeled away. This may be due to the operation of several factors, the significance of which can be only speculative. Perhaps the vinylite resin produces a local inhibitive influence on perspiration or it may have an absorptive action. Whatever the explanation may be, of practical importance is the fact that it has a desirable and bacteriostatic effect.

SUMMARY

1. A brief discussion is presented of the importance of a sterile operative field. Two types of bacterial flora are present on the skin: (1) the transient which is easily removed by a few minutes scrubbing, and (2) the resident which is very difficult to remove.

2. An ideal covering for the operative field should possess the following qualities: (1) impermeability to bacteria; (2) bactericidal action; (3) nonirritancy; (4) transparency; (5) adhesiveness to skin; (6) elasticity; and (7) facile incisability.

3. Vinylite resin fulfilled the requirements in laboratory tests, and was employed successfully in 30 clean surgical cases.

4. Further studies are being carried out at the present time to substantiate its value for this purpose.

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PERITONEOSCOPY

New Applications and a New Supplementary Instrument

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THE peritoneoscope, devised for visualizing the abdominal cavity and its viscera, is similar to the foreoblique cystoscope except that it is larger and uses an air medium, whereas the cystoscope uses water. After preliminary pneumoperitoneum, the sheath and trocar tip are introduced into the abdominal cavity through a small stab wound. The trocar is then removed, the peritoneoscope inserted and an examination made. Biopsies can be taken with a special forceps which carries a small observation telescope. A detailed description of peritoneoscopic technique has been made by Ruddock (9, 10) who, in 1934, devised the instrument now most widely used. This author's last 750 cases without a single mortality testify to the safety of the procedure. Carried out as it is under local anesthesia, it is, furthermore, a minimal operation. As a rule, the patient may be up and around 8 hours after an examination, or the following day if a biopsy has been taken.

I wish to describe a new instrument for assisting peritoneoscopy and to present from my series of 125 cases several new or little exploited applications of peritoneoscopy.

THE NEW INSTRUMENT[1]

The new instrument consists of a blunt tipped rod or "manipulator" and an insulated endothermy electrode, both of which fit into the sheath of a small paracentesis trocar through an airtight rubber nipple (Fig. 1). When needed, the trocar and sheath are introduced through a tiny separate stab wound under peritoneoscopic view, the trocar is removed and the manipulating rod or electrode is inserted. The electrode is capable of dividing adhesions, opening benign cysts, etc. With the rod, obstructions to peritoneoscopic vision are pushed aside or hidden structures lifted into view (Fig. 2). The liver and gall bladder, usually accessible to the peritoneoscope, may either one or both become obscured by adhesions or loops of bowel. These obstructions can be gently pushed one way or another to allow adequate visualization. When overlapping, the edge of the liver can be lifted up to disclose the gall bladder, hidden between it and the colon. The spleen, not often seen by the unaided scope, unless greatly enlarged, can usually be manipulated into view. The appendix almost always hidden by loops of ileum or by the cecum, is easily lifted up for inspection by the rod. In the pelvis, tubes and ovaries are sometimes partly or completely hidden by their prolapsed position, but the tip of the instrument hooked under the round ligament will pull them up into plain view. Sigmoid, cecum, and colon can be pushed about to secure the best visualization.

We have so far used the auxiliary instrument 31 times. There have been no accidents and the results have been gratifying.

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[1]This instrument was presented both in an exhibit and in a moving picture at the meeting of the Southern Medical Association in Louisville, November 15–19, 1940. The diathermy electrode was added 3 or 4 months later. Two other authors in recent publications have independently described instruments auxiliary to peritoneoscopy. Robinson and Fisk use an instrument similar in principle to our own and Lamb described a transparent bladder that can be inflated around the peritoneoscope, thus pushing viscera aside.

NEW APPLICATIONS OF PERITONEOSCOPY

Knowing the potentialities of the peritoneoscope and accessory instrument, the trained peritoneoscopist will come to adapt it to a widening variety of diagnostic and therapeutic problems outside its recognized routine. The following are examples.

Gunshot and stab wounds of the abdomen of doubtful penetration. Heretofore, surgical exploration has been the accepted means of ruling in or out perforation of the parietal

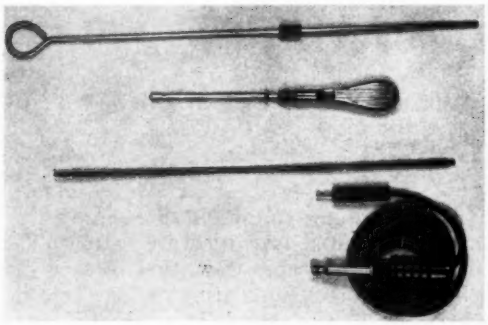

Fig. 1. The new instrument consisting of a small trocar and sheath, manipulating rod, carrying the airtight rubber nipple, and the insulated endothermy electrode and cord.

Fig. 2. The manipulating rod in use.

peritoneum. Peritoneoscopy will give the same information, for by probing the débrided entry wound with a hemostat the suspected area of peritoneum is tented inward for inspection through the peritoneoscope (4).

Prior to our use of the peritoneoscope in these cases, 12 per cent of all surgical explorations of abdominal bullet and knife wounds at the Louisville City Hospital revealed no penetration and hence were unnecessary. Furthermore, well over 90 per cent of these wounds were so located that their penetration or nonpenetration could be reliably determined by means of the peritoneoscope. So far, peritoneoscopy was done in 16 patients with such injuries. In 7 of these penetration was found, thereby indicating immediate laparotomy. The other 9 patients were spared a laparotomy by visualizing an intact parietal peritoneum beneath the entry wound.

Differentiating between appendicitis and salpingitis and between appendicitis and cholecystitis. All are familiar with the occasional female patient who is suspected of having salpingitis but upon whom an exploratory operation is performed "to rule out" an acute appendicitis. In these cases it is our practice first to inspect the adnexae. If they cannot be visualized by the unaided peritoneoscope, they are easily hooked up for inspection by the manipulator. If salpingitis is found, for confirmation the appendix is lifted up on the rod and examined for abnormality. If the tubes are normal and the appendix appears suspicious, laparotomy is performed.

So far, we have used the peritoneoscope in this differential problem 5 times with complete success and with no untoward results. Three times a diagnosis of salpingitis was made and laparotomy avoided, and once the diagnosis of appendicitis was made and verified at operation. Once early appendiceal peritonitis was unexpectedly discovered. The patient was treated conservatively by the Ochsner regimen and made an uneventful recovery. Interval appendectomy 5 months later confirmed the previous diagnosis and revealed normal adnexae.

Rarely a differential problem arises between acute cholecystitis and acute appendicitis. This was exemplified recently on our wards by a 22 year old negro male. Symptoms and signs pointed chiefly to early acute cholecystitis, but an inflamed high lying appendix could not be ruled out. Peritoneoscopy was performed and by this means a distended, injected gall bladder was visualized. Pressure against it through the abdominal wall caused pain. The appendix was then lifted up by the manipulator and found to be normal. The patient's symptoms subsided satisfactorily on a conservative regimen.

Lysis of adhesions and rupture of ovarian cysts. Benedict and others have aspirated ovarian cysts under peritoneoscopic guidance. The only case we could find of peritoneoscopic lysis of intra-abdominal adhesions was reported by Jones in which he divided bands between liver and diaphragm to allow more complete pneumothorax. Since devising the insulated endotherm electrode a year ago, we have encountered only 1 patient suffering from genuine painful adhesions. This was a 44 year old negress with persistent sticking pain beneath the right breast of almost incapacitating severity. Roentgen studies of the chest, gall bladder, and gastrointestinal tract were negative. Peritoneoscopy revealed a normal gall bladder, old pelvic inflammatory disease, and Curtis' "violin string" adhesions between the liver and the anterior abdominal wall and diaphragm. Tugging on these exactly reproduced the sticking pain. The adhesions were divided with the cutting current under peritoneoscopic guidance and after 6 months the pain has practically gone and the patient has returned to work.

On 2 occasions we undertook to rupture follicular cysts of the ovary in young women with severe menorrhagia who had not responded to hormone therapy. The purpose was to remove, if possible, the stimulus for the excessive flow. In 1 patient examined before we had devised our manipulating rod, we were unable properly to visualize the ovaries. At laparotomy subsequently a cyst of the right ovary was found. In the second patient a follicular cyst of the left ovary was found and punctured with the escape of about 2 ounces of straw colored fluid. For 6 months the patient's excessive flow gave place to occasional scant bleeding or spotting and the endometrial biopsy changed from hyperplasia to anovulatory hypoplasia. The patient was so well pleased that when flooding recommenced, she requested another peritoneoscopy. However, the second examination revealed only small sclerosed ovaries and no sign of the previous cyst. The patient is now being given a trial of lactogenic hormone before surgery is resorted to.

Nonpenetrating abdominal trauma when internal injury is suspected. Ruddock (10) and Fry both recommend endoscopy. Nevertheless, we feel that the findings in cases of nonpenetrating abdominal trauma when internal injury is suspected must be interpreted with caution. Peritoneoscopy can safely rule in or out rupture of spleen or liver. However, although the discovery of laceration of bowel or stomach would constitute a clear-cut indication for surgery, the failure to find hollow visceral injury by the peritoneoscope would by no means rule it out.

Peritoneoscopy was performed in the case of 1 boy whose abdominal findings were only mildly suggestive of intraperitoneal hemorrhage following a bicycle accident. The discovery of moderate hemoperitoneum decided us upon surgery. At operation 2 lacerations in the right lobe of the liver were found and repaired. The boy made an uneventful recovery.

Differentiation between bleeding peptic ulcer and ruptured esophageal varix. About 2 years ago we had the embarrassing experience, upon operating for massively bleeding peptic ulcer, of finding instead a typical hobnail cirrhotic liver and, indirectly, bleeding esophageal varices. A few months later we met with a somewhat similar case. This time, though ruptured varix seemed more likely, there were no ascites and bleeding ulcer could not be ruled out. A peritoneoscopic examination was gently performed, revealing a typically cirrhotic liver and thereby removing any question of surgery. It seems that this procedure is less likely to restart or to aggravate bleeding and is more certain in diagnosis than the alternative barium swallow proposed by Schatzki.

SUMMARY AND CONCLUSIONS

We have presented a new instrument to assist peritoneoscopy and have described a few new applications of the procedure to surgical problems with the same purpose in each case, that of avoiding laparotomy.

A number of authors (1, 8) warn against peritoneoscopy in cases of suspected penetrating abdominal injuries and the vast majority give as a contraindication any suspected acute inflammatory condition, such as acute appendicitis or salpingitis. However, in those cases in which exploratory laparotomy is the

only alternative method of deciding whether or not surgery is indicated and in which peritoneoscopy is equally capable of making that decision, I urge that peritoneoscopy be chosen on the grounds that it is much the lesser and safer procedure, seldom incapacitating the patient for more than 24 hours.

Incidentally, 3 of our 4 accidents (bile fistula from liver biopsy in a case of obstructive jaundice, moderate hemorrhage following splenic biopsy in a case of monocytic leucemia, and perforation of ileum in a far advanced case of fibrocaseous tuberculous peritonitis) occurred in generally accepted and what we might term "medical" applications of peritoneoscopy. The only untoward result among the "surgical" uses of the instrument was a mild pneumothorax caused in a patient with gunshot wound of the abdomen in which the bullet also penetrated the diaphragm.

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THE NATURE OF A VIRUS ASSOCIATED WITH CARCINOMA IN RABBITS

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FOR many years, a most interesting phase of tumor research has been the study of a small group of virus-induced conditions which behave in many respects as do neoplasms in general. Until 1933 the principal representatives of the group were leucosis of fowls and the chicken sarcomas. At that time, however, another virus-induced growth was added (13), in this instance, one occurring in mammals, namely, the rabbit papilloma. Papillomatosis of one form or another is of frequent occurrence in man and the lower animals, and the infectious nature of certain types of these growths, chiefly in man and dogs, has long been known. Nevertheless, studies of these conditions from the point of view of tumors were greatly limited because of the character of the diseases themselves or of factors concerned with the host. As shown by results obtained, rabbit papilloma, a mammalian virus-induced growth, has proved to be an excellent material for study in a readily accessible host.

Infectious papillomatosis occurs endemically in western cottontail rabbits and is characterized by the presence of warty epidermal growths. The disease can be reproduced in the laboratory in wild or domestic rabbits by extracts of growths from cottontail rabbits, or, rarely, from those of domestic animals. The papillomatous growths display in many respects the behavior (9) of the typical mammalian neoplasms of unknown etiology. Of great significance has been the finding that the papillomatous growths often undergo radical changes (10), developing with time the typical characters of destructive, metastasizing carcinoma, frequently in domestic rabbits, rarely in cottontail rabbits.

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In its relation to the induction of neoplastic processes in the rabbit, the papilloma virus is a tumor agent of very considerable interest in the problem as a whole. A knowledge of the nature of this agent and its properties has been sought in a direct approach by studies on its isolation and purification. It has been possible to isolate a specific material behaving as the virus from infectious papilloma extracts, and studies have been made on the properties of the purified material.

ISOLATION OF THE PAPILLOMA PROTEIN

The procedures for isolation and purification (1) have proved relatively simple, though time consuming. Warts were gathered in the field from trapped cottontail rabbits and stored in glycerin solution. In the laboratory the growths were ground to a 7.5 per cent suspension and extracted in physiological saline solution. The extract, cleared of tissue débris by filtration through celite or low speed spinning in an ordinary centrifuge, was subjected to 4 or 5 cycles of alternate low speed (at 9000 revolutions per minute or 7000 times gravity) and high speed (30,000 revolutions per minute or 60,000 times gravity) spinning in the air-driven ultracentrifuge. The high speed run was for 45 to 60 minutes, resulting in sedimentation of practically all virus activity. Pellets so obtained were broken up and dissolved in phosphate buffer pH 6.5. The purpose of the low speed run on dissolved pellets was the elimination of insoluble colloidal material packed tightly during sedimentation of the virus and not dissolving when the pellets were broken up.

The yield of material purified in this way has been as high as 1 to 200 and as low as 1 part to 125,000 parts of the initial wart tissue. During 4 years of study, approximately 1 gram of the purified product has been available for examination. The material gives

positive tests for protein. Solutions containing 1 milligram per cubic centimeter are opalescent and milk-like. The results of elementary analysis and fractionation given in a succeeding paragraph show the material to be nucleoprotein containing possibly a very small amount of fat.

HOMOGENEITY AND PHYSICAL STATE OF THE PROTEIN

The problem for first consideration has been the determination of the degree of the purity and homogeneity of the isolated protein in order to establish a basis for evaluating the results of analyses on constitution and behavior. Recent advances in the study of proteins have provided a number of physical tests suitable for application to this problem. Those used singly or in combination have been studies on: (a) homogeneity with respect to rate of sedimentation in the analytical ultracentrifuge; (b) homogeneity of electric charge density as measured by the reversible spread of the moving boundary in the Tiselius electrophoresis apparatus; (c) the rate and manner of diffusion; and (d) the viscosity of the purified protein solutions.

Sedimentation velocity studies in the an alytical ultracentrifuge give information based chiefly on particle shape, size, and mass. Such studies were made in parallel with development of the procedures of isolation. Examination of solutions of pellets obtained in the initial sedimentation in the quantity ultracentrifuge revealed the presence of an ultraviolet light absorbing material with a sedimentation constant of about $S_{20°}$ = ca. 250×10^{-13} cm. sec.$^{-1}$ dynes^{-1}(1). In such a preparation the sedimenting boundary was not entirely sharp, and there was seen also some of the usual tissue protein of molecular size so small that no sedimentation of it occurred in the ultracentrifugal field employed in the study. After 3 to 5 cycles of low and high speed spinning, however, there could be seen only the specific material, all light tissue protein and very heavy insoluble colloidal material having been eliminated. With such a product the sedimenting boundary was very sharp, and, from studies of many samples, the sedimentation constant was $S_{20°} = 278 \times 10^{-13}$ cm. sec.$^{-1}$ dynes^{-1}(8). The sharpness of boundary and freedom of products other than those associated with the specific boundary demonstrate a very high degree of homogeneity of the purified material with respect to this method of study. The examination of other substances by this method has shown that such a degree of homogeneity has been evident only with solutions of a single molecular species. These results, together with the high sedimentation constant, indicate the purified material to be a high molecular weight protein.

Further information of the physical nature and state can be obtained by examination in the Tiselius apparatus. For this purpose solutions containing 2.7 to 4.5 milligrams purified protein per cubic centimeter were studied (11) in the pH region from 3.78 to 7.7, the range in which the material is stable (2). In periods of 5½ to 23 hours, the protein particles migrated with a single very sharp boundary. The symmetry and singleness of boundary and its sharpness or lack of spread revealed a degree of electrophoretic homogeneity which has been seen only with solutions of a few highly purified proteins. These results indicate a remarkable similarity in electrical properties amongst the individual protein particles and thus provide a second and strong indication for the molecular state of the protein.

Evidence for the monodispersity of the protein has been seen in diffusion experiments. The rate of diffusion is a function of the size and shape of the protein particles. The shape of the diffusion curves is dependent on the degree of homogeneity. The experimental curves (8) observed here were of the shape of a gaussian normal error curve, revealing an ideal diffusion behavior and thus high uniformity in the size and shape of the particles. The observed low diffusion constant, $D_{25°} = 6.65 \times 10^{-8}$, was again indicative of large molecular size.

The relative viscosity of a protein solution is a function of particle shape and practically independent of particle size. Studies on solutions of the purified protein showed that the relative viscosity was a linear function of protein concentration. This result is indicative only of normal flow and alone is not an index of the state of dispersion. On the other hand,

the shape factor evaluated from viscosity data agreed with that calculated independently from the sedimentation and diffusion data. In the face of this agreement, the viscosity results can be considered additional evidence of homogeneity.

The results of sedimentation, electrophoresis, and diffusion experiments furnished evidence of a degree of monodispersity of the purified protein equal to that of the most homogeneous proteins studied. From a combination of diffusion with sedimentation and with viscosity data, the shape of the molecule is seen to be that of an oblate ellipsoid with an axial ratio of 11 if hydration is neglected. The density of the material is 1.323, which together with sedimentation and diffusion data gives a value of 47,100,000 for the molecular weight.

RELATION OF THE PROTEIN TO THE PAPILLOMA VIRUS

These investigations have served, within the limits of the methods, to demonstrate the high state of purity of the isolated product and its existence in the molecular state. These tests are based on physical and chemical properties of the protein and serve to show that only one material is present. The problem now becomes that of determining the relation between this purified protein and the virus. The causative agent of the growth is recognizable only by its biological behavior, and a correlation of the properties of the protein with those of the virus can be accomplished solely through biological response in animal experiments. Because of the recognized variation in animal work, the results of biological tests cannot be employed as estimates of physical and chemical homogeneity but can be utilized for judgment of uniformity in behavior. Any correlation of the properties of the protein with those of the virus is dependent finally on the limits of the biological method employed.

The chief biological property of the virus is infectivity or the capacity to induce lesions in the form of warts. It has consistently been found that infectivity is associated with the protein. In numerous experiments, the yield of purified material has been roughly proportional to the infectiousness of the wart extracts from which it was derived. This is strikingly emphasized in comparing results of ultracentrifuging cottontail rabbit warts with those of similar procedures on domestic rabbit growths. Naturally occurring warts from most cottontail rabbits are usually highly infectious. On the other hand, infectivity is rarely seen with extracts of domestic rabbit growths. Despite ultracentrifugation of many liters of extracts of domestic rabbit growths, no high molecular weight protein has been seen.

For studies on specific infectiousness associated with the purified protein, a special method has been developed (3) for its measurement with a relatively high degree of expected accuracy. Employing nitrogen content as an index of protein quantity, there has been found a linear relationship between the logarithm of protein amount and the incubation period in days of warts induced with it. With this procedure, many samples of the protein have been found highly uniform in their degree of infectivity. The infectious unit of protein, in terms of that quantity of it required to produce lesions at 50 per cent of the spots inoculated, is $10^{-8.355}$ grams (4). As a routine procedure, the volume of inocula has been 0.1 cubic centimeter of protein solution. From the molecular weight it has been calculated that this infectious unit is comprised of an average of 56,800,000 molecules in 0.1 cubic centimeter of inoculum. The uniformity of behavior is shown in the results seen with several different batches of material which have given infectious units of $10^{-8.355}$, $10^{-8.285}$, $10^{-8.3}$, and $10^{-8.368}$ grams. These findings, as determinations of virus infectivity, are in exceedingly close agreement. Another biological method used was complement fixation which gave results (6) of uniformity paralleling those with infectivity. Perhaps the most satisfying demonstration of uniformity is the quantitative nature of the serum-protein relations in the neutralization reaction (5). The constancy of the results is such that the reaction can be expressed mathematically with high accuracy.

Further evidence is available of close relationship between the protein and the papil-

loma virus. This is especially illustrated in parallel studies (2) on molecular stability of the protein and virus infectivity with respect to hydrogen ion concentration. Molecular stability is at a maximum between pH 2.9 and 10. This is likewise the region of maximum stability of virus infectivity. In solutions more acid than pH 2.9, the molecules disintegrate, as shown by analytical ultracentrifugation, and here infectivity is lost immediately. In the alkaline range, however, infectivity is immediately lost at pH 10 whereas molecular disintegration begins quickly only at pH 10.2 or above. The isoelectric point of the protein is at pH 5.0 where the protein is insoluble. Here the protein precipitates, and with it are carried the infectious qualities of the solution.

The foregoing results serve to establish with reasonable certainty the identity of the purified papilloma protein and the papilloma virus. The experimental findings thus can be interpreted as describing the properties of this infectious agent. Elementary analyses (1) have shown the virus protein to contain carbon, 49.6; hydrogen, 7.2; phosphorus, 0.94; nitrogen, 15.0; and sulfur 0.22 per cent. There is present 6.45 per cent carbohydrate. The possibility of fat as a conjugated constituent is still not entirely clear. Early fractionation with small amounts of material gave 3.2 per cent lipoid. More recent investigation (18) has indicated a value of 1.49 per cent. Fractionation (18) has revealed the presence of nucleic acid to the extent of about 8.0 per cent. The nucleic acid is definitely of the thymus type, there being no detectable trace of ribose or yeast nucleic acid.

EVALUATION OF STUDY

In the experiments described, a specific material exhibiting the biological characters of the rabbit papilloma virus has been isolated from infectious extracts of growths from cottontail rabbits. This component of the growths fulfills the criteria of a homogeneous macromolecular nucleoprotein which may or may not contain a small quantity of conjugated fat. The evidence thus far obtained indicates that this macromolecular material is the papilloma virus.

For present interpretations, the results of these investigations of the causative agent of the rabbit papilloma are best considered in comparison with the findings on other filterable viruses rather than other tumor agents. During the past few years, much attention has been given to studies on the isolation and properties of viruses, both those causing disease in plants and those pathogenic to animals. In 1935 Stanley (15) announced the isolation of a high molecular weight protein from plants diseased with tobacco mosaic virus. This material, obtained by classical methods of chemical fractionation, is crystalline, and its identity with the virus of tobacco mosaic disease has been well established. Subsequently, with access to the newly developed air-driven ultracentrifuge, numerous other plant virus proteins (16) have been isolated, and all thus far studied possess properties ascribable to entities existing in the molecular state rather than those to be expected of individuals classed as bacteria. Similar studies in the field of animal viruses have proceeded much more slowly. It has been possible to concentrate and to purify to a considerable degree a number of these agents. Only a few have been procured in amounts and in a state suitable for study, namely, the elementary bodies of vaccinia (7), the rabbit papilloma virus and the agent of equine encephalomyelitis (12). The criteria for judging the nature of these 3 viruses, however, are not applicable to the same extent for each of the three. Chemical analyses of vaccinia elementary bodies have given fairly uniform results. Microscopic examination has been employed for interpretation of homogeneity of purified preparations, but the findings can hardly be considered quantitative and further provide no indication of the nature of the bodies. Numerous studies have been made on the bodies in the analytical ultracentrifuge, and those workers (14) having the widest experience have reported spread in the sedimenting boundaries indicating lack of uniformity in particle size. The elementary bodies are not of a nature suitable for electrophoresis studies by the moving boundary method (14) and other tests have not been applied. The results as reported cannot be employed to place the

elementary bodies definitely in either the category of molecular or that of bacterial entities. Considerably better evidence is at hand of the nature of the equine encephalomyelitis virus. Sedimentation diagrams (17) of the purified material show the sharp boundary of molecular substances. None of the data thus far obtained are incompatible with the view that this virus also is molecular.

In striking contrast to the findings with these other animal viruses are those with the papilloma virus protein. Here many of the rigid criteria of the physical state of proteins in general are applicable, and in all instances the results have consistently demonstrated the homogeneity and the molecular nature of the protein. The papilloma protein is thus at least one animal virus which can be grouped with assurance with the macromolecular plant virus nucleoproteins.

SUMMARY

The isolation and properties of a specific material from virus-induced cottontail rabbit papillomas have been described. This material, which behaves biologically as the virus responsible for the disease, is a nucleoprotein obtainable in solutions of high homogeneity. Its physical properties with respect to sedimentation, electrophoresis, diffusion, and viscosity are those of a molecular substance. The values obtained in such studies indicate a molecular weight of 47,100,000. With respect to the physical state, this animal virus falls into the same category as occupied by the macromolecular plant virus nucleoproteins.

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THE GENERAL SURGEON'S APPROACH TO THE PROBLEMS PRESENTED BY FRACTURES AND OTHER TRAUMAS

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PROBABLY many question the need for a discussion of a subject which seems to have been settled for some time by the orthopedists and the patients. In urban, most suburban, and even in the rural districts, the patients themselves are consulting the orthopedists directly for the treatment of fractures, thus short circuiting the traditional route via the general practitioner, the general surgeon, while, for the correction of resulting permanent deformities, the orthopedist has a clear field.

This is a general statement, and the practice varies in different parts of the United States and Canada, but it would seem fair to say that it is only in the older parts of our land, in the regions where one finds the litter of antiques and traditions persisting, the general surgeon still has the undisputed privilege of treating fractures. If this is the trend of the times, is it right or wrong; and if wrong, what should or could be done about it by the general surgeon?

Is the specialization of surgery rational, necessary, or in the best interests of the patient? I feel sure we are on common ground when claiming that irrespective of our personal interests it will be the welfare of the individual patient which will, and should, govern the practice of medicine and surgery in the future.

Some years ago I discussed this subject with Dr. Meeker, then dean of the Graduate School of Medicine of the University of Pennsylvania, and from what I have already said you will understand my side of the argument. I was not convincing him by any means, and finally, a little heatedly, I asked if he would define a specialist. He quickly and positively replied, as he usually does, "a specialist is a surgeon or an internist who can and does one thing well, and does it better than any one else." Again upon my request for his definition of a general surgeon, his answer came just as promptly as before, "a general surgeon is one who does not do any one thing particularly well."

The passing of time has softened to some extent my immediate resentment, so much so that I am offering his definition as a text for our consideration.

You will note that Dr. Meeker said "*does not* do any one thing particularly well." But he *did not say* "*cannot.*" This seems to me to open the way for our discussion.

Is it true that the lay public (for Dr. Meeker is not a doctor of medicine, but a doctor of philosophy in biochemistry) agree that general surgeons do not do any one thing particularly well; and if so, why? Is this attitude toward fractures much different from that which they have toward other specialties including: obstetrics and gynecology; genitourinary surgery; neurosurgery; facial maxillary surgery; plastic; thoracic; and one of the latest diseases of the peripheral vascular systems?

In many of the medical schools at the present time all these fields of surgery are being taught by specialists, not by the general surgeons, and is it any wonder that the graduate medical student, when he becomes a practitioner, refers his traumatic surgery, or at least his fractures, to the orthopedist? This being so, and if the orthopedist does not give as good service to the patient as the general surgeon, will this practice continue for long? I doubt it, for sooner or later the patient, or his family doctor, will properly evaluate the services received.

By this indirect approach we come, to the crux of the situation, as expressed by Dr. Meeker. *Does* the general surgeon give to the fracture patient as good or better service than the orthopedist? I shall deliberately avoid

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giving my answer to that question for the time being.

The next question then: *can* he provide, as a result of his training and experience in general surgery, as good or better service than the orthopedist? I am positive that he can and should.

My thesis, then, is: that the general surgeon, because of his broad surgical training, should be able to compete successfully with the orthopedist in the care of trauma of the soft tissues, bones, and joints, but I have a feeling that he is not holding his own at the present time.

Recently a new specialty has been developing, that of traumatic surgery, composed of general surgeons who are interested in fractures, and orthopedists who are interested in the general problems of trauma. This may be the answer to the dilemma, for in such a group we find surgeons who are particularly interested in the treatment of traumatic conditions, and orthopedists who are willing to admit that they need a much broader training in the care of trauma than is provided by a limited experience in the regional field of bones and joints. It may be that the surgeons of South America have already solved this quandary, for during a recent conversation with Dr. Juan M. Allende, professor of clinical surgery in the University of Cordoba, Argentina, he told me that the surgery of trauma in South America is carried on exclusively by specialists, and the specialty is known as the surgery of traumatologia and orthopedia.

My effort tonight will be to call your attention to these changing conditions in the surgery of trauma in this changing world, and try to interpret them from the viewpoint of the general surgeon.

Interest in major trauma is being constantly stimulated in these days by military, industrial, and automobile catastrophes. During a similar crisis, under the pressure of the first World War, improved methods of fracture and wound treatment were instituted. Some of these methods, in the original or modified form, were promptly incorporated into the accepted lore of surgical treatment, while others have been discarded long since, for example, at the present time the elimination of Dakin's solution from the United States Pharmacopeia is being discussed seriously.

1. We are now faced with the probability of having to care for large numbers of war casualties, and it is apparent that in this war the surgical problems will be more complex than in the previous wars. The absence of well defined battle lines, and the use of air armadas and panzer units, which attack the civilian population over large areas of a country, spreads the casualties to the noncombatant population. In the present European struggle it is reported that civilian casualties have been ten times more numerous than have military, as a result of the bombing and shelling of cities. There are new types of injuries, and the wounds caused by the modern high explosive shells and bombs, whose fragments have terrific velocity, tend to be massive and more devastating than the wounds of former wars. The blast injuries resulting from bombs of this type require attention which was not even suspected in the last war (Fig. 1). They result from a high pressure wave, which is immediately followed by a low pressure one, and the injuries usually take the form of capillary hemorrhages of the lungs (Figs. 2 and 3), the liver, the spleen, intestines, adrenals, and kidneys.

2. A second reason for particular interest in the problems of fractures and trauma at this time is the increasing pressure being exerted by the economic front of the workmen's compensation legislation. Methods of treatment which will insure the ultimate restoration of function in the minimum length of time are now demanded by the compensation boards and insurance companies. This has led to higher standards of reduction, fixation, and after-treatment of fractures. This trend is also directly responsible for more widespread employment of open reduction and internal fixation. Though internal fixation was strongly advocated many years ago by Arbuthnot Lane, the difficulties of the technique and the meticulous equipment in personnel and material incident to the proper attainment of this type of fixation discouraged its general use. Only recently have we realized the vital importance of the rigidity provided by internal fixation, which makes possible active motion

Fig. 1. Wounds of the face resulting from high explosive bombs. (Courtesy of Mr. Broster.)

of the affected extremity immediately after the operation. This ideal can now be obtained through the employment of the biplane fixation which was devised by Clay Ray Murray of New York.

As internal fixation became more generally practiced, it was quite evident that improvement was necessary in the type of metals used. The plates and screws became eroded and would lie loosely on the bone fragments. It was Venable and Stuck who demonstrated that this erosion was due to the electrolytic action of tissue fluids upon the metals. They claim that when any two dissimilar metals are used as fixatives in the same wound, an electrolytic process is set up between these metals in accordance with the laws of electromotive force. Vitallium was proposed by them as a metal entirely inert to the effects of body fluids when not associated with any other metallic substance. As a result of this research vanadium has been discarded as the standard metal for plates and screws, and in its place vitallium, or high-chrome low-nickel steel, or tantalum are now in vogue.

3. Motor accidents provide the third need for increased interest in fractures and traumatic wounds. More stringent traffic regulations of all kinds are needed to stop this terrible waste. It is without question the responsibility of the medical profession, and surgeons in particular, to see that this evil is corrected. Legislation, publicity, and the direct fostering of organizations such as the Red Cross, together with the guidance of state highway commissions in instructing laymen in the proper methods of administering intelligent first aid care to the victims of industrial and automobile accidents, are necessary to promote the interest of the laity in the subject.

A sign encountered this summer while motoring through New England indicates the responsibilities which motor accidents are bringing to the rural physician and surgeon, and the economic burden being thrust upon communities, many of which are unequipped and financially unable to bear them. A large billboard, was found at the entrance to the town, which read: "This town does not maintain a hospital, and motorists are warned that they should take every precaution to avoid accidents while driving through, for we are not equipped to take care of them." This may be the easiest way out, but I am sure it will not be the final answer, even in that town. Nor should it be.

During September, 1941, 3,777 persons met death as a result of motor accidents in this country. This was an increase of 14 per cent over the same period last year, and marks the fourteenth successive month to show an increase over 1939 and 1940. With 1941 three-quarters gone, the total killings have been 27,860, which is a rise of 17 per cent over the fatality list for the same period of 9 months in 1940.

After this brief consideration of some of the many special fields of knowledge which must be mastered in order to cope with the changing problems in the treatment of traumatic wounds and fractures, one might think that we had forgotten our original promise. On the contrary, it is exactly because of the complexity of these problems that we believe that a general surgeon, employing the basic knowledge of the principles of surgery, should be better

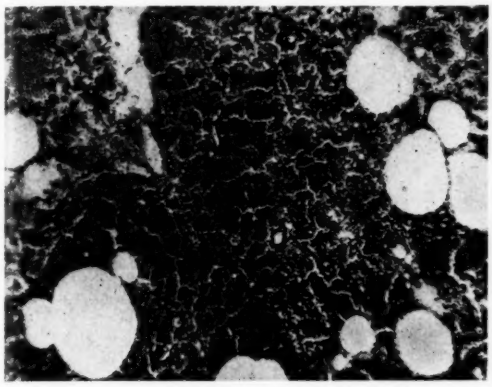


Fig. 2. Low power view of lung of a woman killed in a steel shelter as the result of a "near miss." There was massive hemorrhage throughout the left lung. × 58. (H.L. 3). (Courtesy of Mr. Broster.)

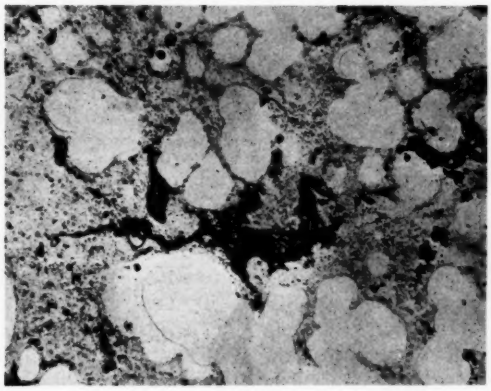


Fig. 3. Section of the lungs of a woman killed in an air raid. The casualty was extricated from the remains of her house, and autopsy revealed numerous hemorrhages in both lungs. The specimen has been stained with scharlach R (black regions) to demonstrate fat. × 58. (H.L. 5). (Courtesy of Mr. Broster.)

fitted to arrive at a complete solution of them than are his more highly specialized colleagues.

FIRST AID

I feel sure no one will disagree with the statement that the first essential in treating a patient suffering from a fracture or trauma is to try to evaluate the condition of the patient as a whole, and not to concentrate entirely on the local wound or deformity, immediate or final. Age, sex, physical development, nutrition, emotional status, all of these elements and many more must be grasped at the same time as one prepares to administer proper first aid care. I say proper first aid care because—while the beneficial effects of such aid as immediate splinting of fractures or dressing of wounds is unquestioned—the methods of carrying out this first aid may be far from ideal.

May I offer here the slogan which we advocated and taught to the lay public during the last war, and to Red Cross groups during the interval between the two wars, namely, when in doubt as to what you are dealing with, do nothing, and when you are not sure about what should be done, even though you know the indications, do nothing. Those of us who do not see these patients until after the administration of well intentioned first aiders know too well that the patient too often would have been in better condition if he had been left alone and had not received the treatment given to so many of them. Dr. William Darrach has expressed this in a more scholarly way: "In our early examination and treatment we should be guided and restrained by our realization of the pathology, by the mental picture of what has actually occurred beneath the skin, and what may occur as a result of our first aid efforts."

Gentleness is unquestionably the keynote of first aid care and must be rated above all other considerations in the management of severe accident cases.

Hemostasis. In dealing with traumatic wounds it is frequently necessary to control hemorrhage. This is accomplished most easily and with the greatest safety by applying a pressure dressing. The latter should be firm, but not excessively so. Tourniquets are sometimes required to control more severe hemorrhage, but only as a last resort, and one must not forget that periods of release are required if the band remains in place for more than 30 minutes. Gangrene is still too often the result of the application of tourniquets by conscientious first aiders.

Asepsis is secondary only to the control of hemorrhage in the primary treatment of open wounds. As a first aid measure the application of a sterile or mechanically clean dressing is the best safeguard against infection. Anti-

TABLE I.—SHOCK

Cause	Treatment
Hemorrhage	Transfusion
Dehydration	Fluids
Pain	Morphine
Cold	Warmth
Fear	Reassurance
Asphyxia	Oxygen
Exhaustion	Rest

(Courtesy of Dr. Norman E. Freeman.)

septics probably do more harm than good when introduced into a potentially infected wound. Cleansing of the skin area around the wound should be left for the operating room inasmuch as proper solutions and the facilities for using them will probably not be available at the locus of the injury.

Simple methods. There is a tendency among general surgeons who treat many traumatic wounds to utilize relatively simple and conservative methods. Soap and water cleansing of the skin surrounding a wound and irrigation of the wound proper with normal saline solution or sterile water should be used more often than complicated antiseptic skin preparations and antiseptic irrigants. Wounds of soft parts of the extremities should be splinted, not only to prevent pain and hemorrhage, but also to discourage the spread of contaminating bacteria.

What appears now to be an epochal contribution in the control of infection in traumatic wounds is the experimental work of Trueta, which was undertaken with the object of explaining the localization of wound infection when the traumatized tissues were primarily immobilized in plaster. In two series of dogs, one being used for control and the other for experiment, the extremities in both groups were traumatized, the soft tissues lacerated, and the bones fractured. The injured tissues were then inoculated with the Bacillus welchii perfringens and hemolytic streptococci. Following this the wounds were filled with sulfanilamide powder and packed open with vaseline gauze. In the control group the traumatized extremities were not immobilized, while in the other group they were encased in plaster casts.

In the control group every animal died from a gas bacillus infection within 3 days, while in the other group no deaths occurred. Trueta explained this by the fact that the immobilization of the soft tissues resulted in stagnation of the lymphatic circulation. In the tissues of the animals examined after death he found, in the group with freely moving extremities, the previously injected bacteria or their offspring had entered the blood stream within 24 hours after receipt of the injury. In the group in which the tissues had been immobilized, the organisms remained within a short distance of the traumatized tissues but had not entered the lumen of the blood vessels.

FRACTURES

In the treatment of fractures the simplest technique which will afford adequate reduction and complete immobilization should be chosen. Open reduction with internal fixation is recognized as an ideal procedure for the treatment of simple fractures, but should be reserved for exceptional cases. Furthermore, unless one has occasion to practice open reduction with internal fixation frequently, we believe it is better not to attempt this procedure. It is usually not performed successfully by the occasional operator.

In summary we will repeat that our endeavor in treating traumatic wounds is to avoid intricate or cumbersome techniques and to adhere carefully to the fundamental principles of gentleness, hemostasis, asepsis, and immobilization.

It may be well to insert at this point a word about one phase of the treatment of fractures and traumatic wounds which has troubled the surgeons who form the Fracture Committee of the American College of Surgeons, namely, the need for an *educational program* aimed at improvement in the care of trauma of all kinds.

Such a program must have its origin in the *medical schools*, where more emphasis should be placed upon the recognition and management of various types of fractures and traumatic wounds. Furthermore, medical students should be taught to recognize the types of cases which *they will not be qualified* to handle as general practitioners and which should be referred to one specially trained in surgery. In order to accomplish these aims

more time must be allowed by the schools for the teaching of traumatic surgery, and fresh material of this sort should be made available to the students. As far as we know, Dr. Gallie of the University of Toronto was among the first to recognize this need and to make an effort to meet it.

The important elements of this subject cannot be learned in lectures and in dry clinics by viewing the bandaged wounds and splinted extremities. Students must see, and participate, if possible, in the whole procedure from the time the patient enters the hospital until his wound or fracture has been treated and he has been put to bed on the ward. In hospitals, internes and residents require special instruction in this field, and this can be made possible by spending a specified time on a traumatic service. The special value of a traumatic service has been proved to our satisfaction, and in such a plan the traumatic cases are segregated into special wards and cared for by a group of nurses and attendants specially trained in handling the equipment and problems incident to fractures and major injuries. Probably this ideal cannot be achieved generally because of the financial outlay which it entails. However, it is usually possible, at least, to practice a modified version of the idea by having traumatic cases under the care of the same surgeon or group of surgeons continuously for a period of 6 months, or preferably a year. In this way the plan of treatment undertaken is not as likely to be interrupted as when the direction of the service is changed at shorter intervals. Upon discharge from the hospital it is also advantageous to have the same team to carry on in the out-patient department. Both fractures and major traumatic wounds are treated intelligently only if they are followed carefully for prolonged periods after discharge from the hospital. The results of epiphyseal injuries, shortening or tilting of long bones, restoration of joint function, and contraction of scars, to mention only a few instances, cannot be evaluated fully until at least one year after the actual treatment has ceased. Such an organization may seem cumbersome and unwarranted to those who have not seen it in action. This may be true for a short time after its inception, but once established the results are so greatly improved that the satisfaction to both the patient and the surgeon is a sufficient stimulus and compensation to keep it running smoothly.

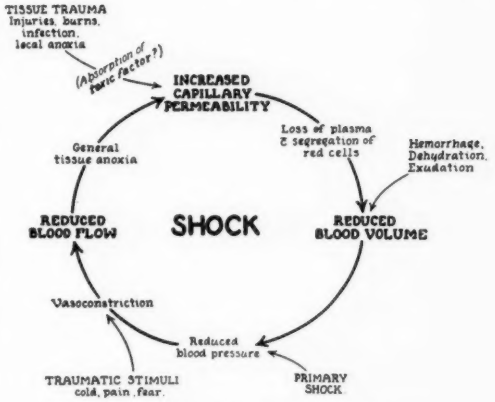


Fig. 4. Courtesy of Dr. Norman E. Freeman.

Undoubtedly one of the most perfect demonstrations, not only of the possibilities but also of the efficiency that can be obtained by the specialization of the surgery of trauma and fractures, is to be seen in the fracture service of Darrach and Murray at the Medical Center of Columbia University in New York. In referring to such an ambitious plan for the teaching of undergraduate, graduate, and postgraduate surgery of this type, one must pay homage to this contribution to the problems of traumatology.

Time will not permit of an exhaustive discussion of the many interesting phases of this subject. However, we have chosen three, namely, shock, burns, and compound fractures, for more detailed consideration.

SHOCK

In the discussion of shock the general surgeon must always define his understanding of the pathology of the process in order to justify the type of treatment used (Table I, Fig. 4). We subscribe to the now generally accepted theory that shock is caused by one, or several, or all of a group of factors operative at the time of the injury. These factors are hemorrhage, dehydration, pain, cold, fear, asphyx-

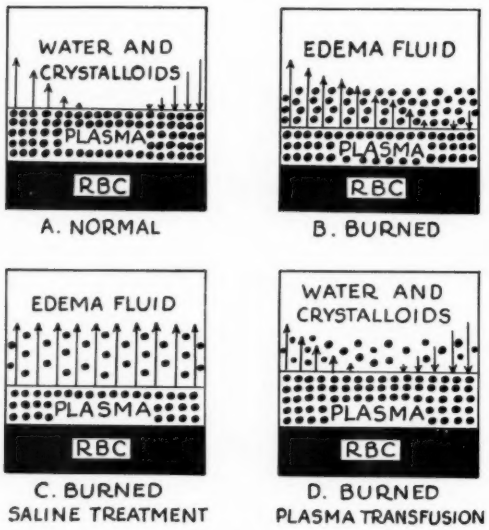


Fig. 5. Distribution of fluid between the capillary and tissue spaces.

ia, and exhaustion, as outlined by Freeman. The total effect of this phenomenon is to produce tissue anoxia which gives rise to abnormal capillary permeability. Consequently there follows a loss of blood plasma, a diminished blood volume, lowered blood flow, blood stasis in the capillaries, and finally, a greater degree of anoxia of the tissues. In this manner a vicious circle is established which can be broken only when the proper treatment is administered.

Treatment of this condition, up to very recent times, consisted of relieving the objective symptoms by means of well known methods.

About 10 years ago the intravenous infusion of saline and glucose was added to the armamentarium. This resulted in a temporary rise in the blood volume and blood pressure which was not sustained because the fluid left the leaking capillaries almost as fast as it was introduced, and carried with it the vital serum protein, so that the harm which was done was not only passive but was likewise active (Fig. 5).

Following this routine use of saline and glucose, whole blood was infused into veins in order to raise and maintain for a length of time the flagging blood pressure. It is true there are definite indications for the use of whole blood in shock, particularly when it is associated with hemorrhage, but the difficulty in performing transfusion into the collapsed veins of the shocked state have been experienced by every surgeon. In this connection we wish to call attention to the recent work of Tocantins, in Philadelphia. During

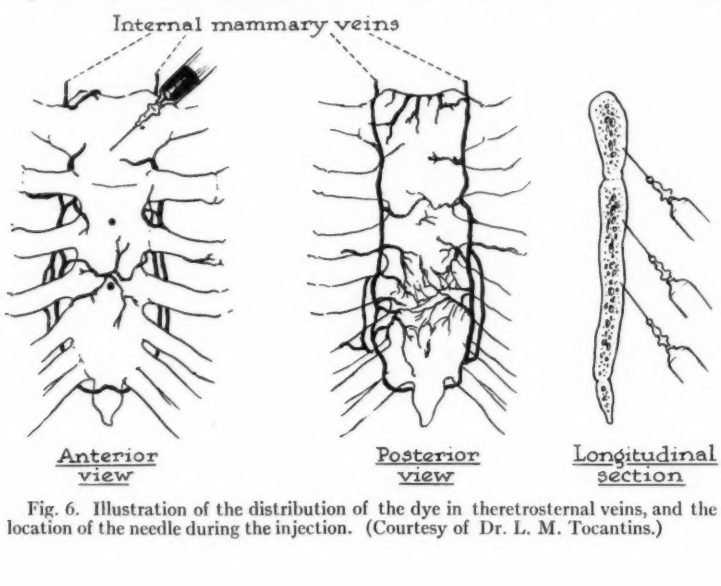


Fig. 6. Illustration of the distribution of the dye in theretrosternal veins, and the location of the needle during the injection. (Courtesy of Dr. L. M. Tocantins.)

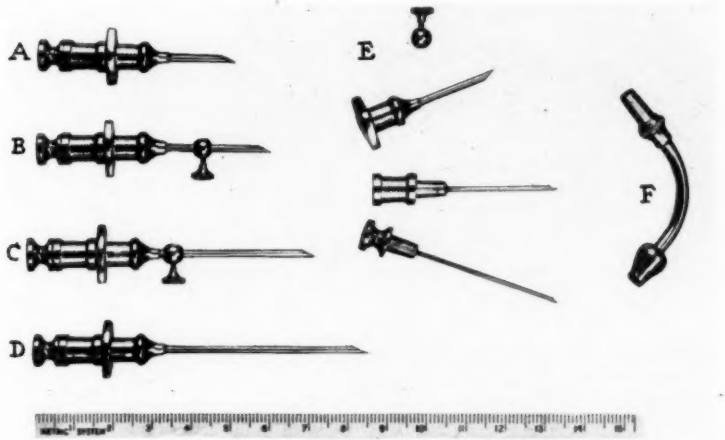


Fig. 7. *A*, *B*, *C*, *D*, infusion needles of various lengths. *E*, component parts of a needle, from top to bottom: needle guard, external needle gage 15, internal needle gage 18, solid stylet. *F*, curved adapter. (Needles made by the George Pilling Co., Philadelphia.)

the stage when fluids are most urgently needed, the physician is left without ready access to the central portion of the circulation because of the collapse of the peripheral veins as a result of shock. It occurred to Tocantins that under such conditions the bone marrow offered the ideal site for the introduction of fluids until the patient reaches such a stage that the peripheral circulation is restored and access to the veins is again possible. Since the marrow veins are surrounded by a rigid envelope, they are less likely to collapse, and probably can withstand forcible injection, without overdistention and leakage, better than the poorly supported peripheral veins. Further, substances injected into the bone marrow cavity are taken up almost immediately into the venous circulation and apparently unchanged (Fig. 6).

"We have experimentally demonstrated this by the injection of dye into the marrow of the sternum of a cadaver and found that it rapidly appeared in the right auricle. The comparatively short distance between the sternal marrow and the right side of the heart makes this possible. The rapid introduction of fluid into this side of the heart may, therefore, help to restore the cardiac output during the phase of acute peripheral failure, by increasing the volume of the blood returning to the central portion of the circulation."

Tocantins needle (Fig. 7). After the needle has been inserted through the cortex and the marrow has been obtained by aspiration, the syringe containing the material to be administered is connected with the needle and the material is injected as fast as the resistance offered to it will allow. In conscious patients, if the fluid is injected at a rate greater than 10 cubic centimeters a minute, there is usually a feeling of fullness in the sternum which, however, passes off immediately upon cessation of the injection. By using a two-way valve, one side connected by rubber tubing to the container of the fluid and the other leading from the valve into the sternal needle, it becomes unnecessary to remove the syringe from the sternal needle every time it has to be filled. In some instances, in which a more rapid rate of injection is desirable, two needles can be introduced into the sternum, one at either end, and since the marrow cavity of the manubrium and the marrow cavity of the sternum seldom communicate, it is possible to inject material through one orifice without it coming out of the other. This method can be used for the administration of any type of medicaments to patients with acute circulatory fail-

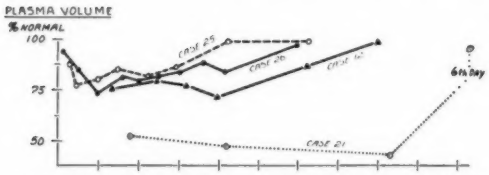


Fig. 8. Illustration of the shifting of the plasma volume in a series of burns which received local treatment only.

ure, and it has been found to be much more efficient than when the material is injected by other routes.

In the 72 cases in which this method was used by Tocantins, no untoward reactions of any kind were experienced.

But there are definite contraindications to the use of whole blood transfusion to combat shock which are readily understandable if one accepts the etiology of shock as outlined here. Whole blood infusions will provide an increase in blood volume, but they also supply an element which is detrimental in shock; the red cells which when added to the circulation serve to increase the viscosity of the blood and thus cause greater capillary stasis. This in turn brings about a greater degree of anoxia and increases the capillary permeability. To put it briefly, whole blood transfusions are contraindicated in shock because they tend to exaggerate the existing hemoconcentration. Hemoconcentration, however, may be absent and not marked when shock is associated as the result of hemorrhage.

The search for a substitute for whole blood, which would raise the blood pressure by increasing the blood volume without increasing hemoconcentration, was terminated happily when the use of blood plasma was suggested. As early as 1927 Strumia first advocated the use of blood serum in shock treatment, but adverse reactions, since found to be due to the absence of the fibrin fraction, caused serum to fall into disrepute. Then in 1929 he found that plasma was equally effective in combatting shock and did not give rise to reactions. Ten years were to pass before the plasma transfusion was widely accepted and employed in shock treatment, but now this therapy is well established. It has stood the test of the demands of war surgery and answers the physiological requirements of the damaged

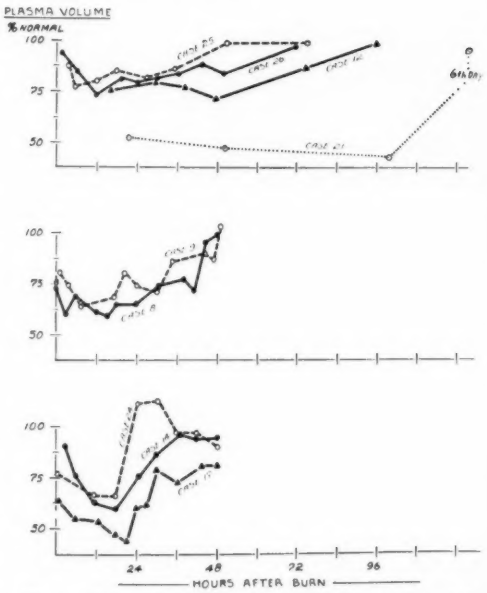


Fig. 9. Comparison of the duration of the shifting of the plasma into the perivascular tissues. Above, When local treatment only was used. Middle, when local treatment and blood transfusions were used. Below, when local treatment, blood transfusions, and adrenal cortical extract were used.

tissue. Plasma dilutes the concentrated blood of the capillaries and tends to remain in the vascular bed better than any other material thus far used.

The history of the production of plasma for infusion in shock states is interesting but too lengthy for consideration here. The preparation of plasma from citrated blood is now accomplished both by centrifuging and by the simpler natural settling process. After preparation the plasma is probably best used in its liquid form, although dried and frozen types of plasma are available. One other interesting development has arisen from this plasma industry. Plasma, once an incidental dividend of the blood bank system, has now become the capital of that system. The demand which is made for plasma is now commonly stated as being four times that for whole blood.

When the use of plasma in the treatment of shock was generally established, it became necessary to discover some way of testing

Fig 10. Interference with the circulation of the hands and digits following the use of tannic acid in the local treatment of severe burns.

clinically for the presence and degree of shock in order to determine the dosage. The laboratory tests devised for this purpose consist of the usual hemoglobin and hematocrit determination and red blood cell counts. From a consideration of these figures the state of hemoconcentration may be determined.

More recently these values have assumed added importance in that with them one can compute by means of a simple formula the amount of plasma lost. Thus replacement of plasma is removed from the realms of uncertainty and carried out on a definite volume basis. An example of such a formula is that of Black which is given as follows:

$$\frac{HB}{100} \qquad \frac{5}{5\text{-}X}$$

HB is the observed hemoglobin
X is the plasma lost in liters.

This formula has been criticized from the point of view that it fails to take into account the fact that the hemoglobin may be very low in shock associated with hemorrhage in which there occurs a compensatory dilution of the blood. However, the formula has been of great value in emergencies and especially in war conditions when one cannot wait for or obtain more complicated tests. If the formula cannot be recalled it is a safe rule to give plasma to any patient in a shock state when the hemoglobin is found to be above 100 per cent.

When laboratory facilities are available for determining the hematocrit and plasma protein concentrations, we have found the following formula devised by Elkinton, Wolff, and Lee to be more accurate than that of Black.

For calculating this quantity, the authors have proposed the following formula:

$$\text{Plasma protein requirement in grams} = 3.5\ W - \frac{W\ (100\text{-}Ho)\ Hn\ Po}{2\ (100\text{-}Hn)\ Ho}$$

W = body weight in kilograms.
Hn = normal hematocrit value, per cent cells.
Ho = observed hematocrit.
Po = observed plasma protein.

If the plasma protein requirement in grams is multiplied by 14 the required volume in milliliters of plasma is obtained.

Fig. 11. Second and third degree severe burns of the forearms and hands, treated with tannic acid, on the right, and with triple dye, on the left.

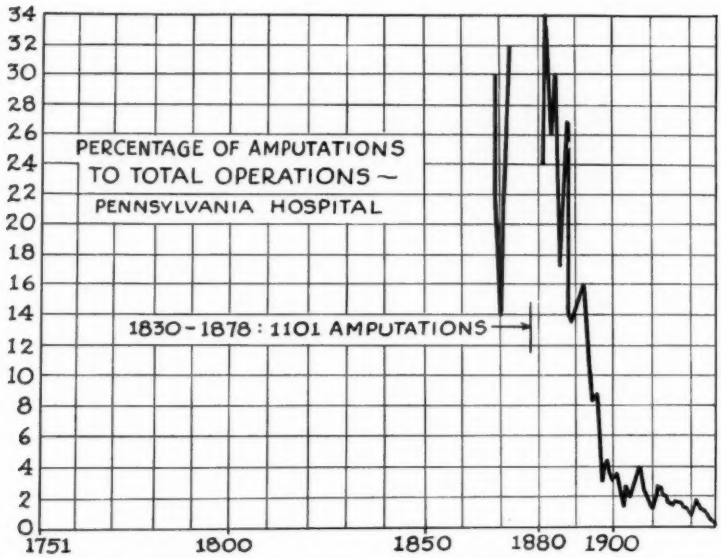


Fig. 12. Illustration of the total number of amputations performed yearly at the Pennsylvania Hospital before and after the introduction of Listerism.

Our final thought regarding shock concerns the use of adrenal cortical hormone in shock therapy. The work of Wolff, Rhoads and Lee suggests that cortin in the form of eschatin has a beneficial effect in combatting the secondary shock encountered in severe burns. This effect is experienced only when adequate plasma is given by infusion at the same time. It is believed that the eschatin does not increase the plasma volume per se, but that it acts by reducing the permeability of the capillaries so that plasma leaks from them less rapidly. Since this therapy is effective in shock produced by burns, we believe that it would also be beneficial in secondary shock caused by other trauma. We plan to use eschatin along with plasma in all cases of traumatic shock encountered henceforth.

BURNS

Extensive superficial burns present an especially complicated problem for the traumatic surgeon. Usually the patient is suffering from secondary shock when he is first seen. As the great majority of burn deaths are still due to this cause, treatment must first be directed toward the prevention and replacement of plasma volume. In the past it was estimated that 80 per cent of the mortality from burns occurred during the first 7 days. The fact that but 1 of 40 consecutive patients, in whom we used plasma and cortical extract, has died in this period would seem to suggest the former mortality rate is now unjustifiable. However, as the later course of the patient will be largely conditioned by the amount of infection which develops, it is also of vital importance to protect the patient from contamination by the immediate use of aseptic precautions (Fig. 8).

Experience has shown that large transfusions of plasma in the early stages accelerate the rate of plasma loss so that a slow infusion is mandated during the early stages. Without the administration of adrenal cortical extract, large infusions were for the most part passed into the perivascular tissues of the patients studied at the Pennsylvania Hospital during and up to the 40th hour after receipt of burn. In the recent cases that were treated with adrenal cortical extract in addition to plasma it was possible to use large infusions effectively between the 18th and 24th hours so that the hematocrit could be restored to normal at this early time (Fig. 9).

Fig. 13. Illustration of the influence of antisepsis and asepsis and the total number of operations performed at the Pennsylvania Hospital before and after the introduction of Listerism.

The local treatment of burns, after a long period of standardization with tannic acid, is again in a state of flux. Current opinion suggests that tannic acid is satisfactory for burns of flat, relatively immobile surfaces, but that it should not be used on the face, hands, or feet because of the danger of circulatory interference if the eschar completely encircles the digits or extremities (Fig.10). On the latter gauze packs saturated with normal saline solution, well padded and held in place by circular pressure bandages, seem to be more satisfactory, according to Koch and Mason. In our experience powdered sulfonamides have proved of value in controlling infection of granulating surfaces preparatory to grafting (Fig. 11).

Regarding skin grafting we would like to emphasize the necessity for early grafting. Whether the skin defect has resulted from a burn, or another traumatizing agent, every effort must be made to replace the lost skin as soon as possible; that is, as soon as the granulating tissue base is surgically clean, but not necessarily aseptic.

The best type of graft for general use is the split graft provided by the Padgett dermatome. This ingenious machine demands careful attention to details in its manipulation, but when its use has been mastered the grafts obtained warrant the time required to acquire the technique. Its chief advantages are the ability to deliver a graft of the exact thickness and size required, and also to deliver grafts of uniform thickness throughout. These are attributes not achieved by the most expert advocates of razor grafts. In cases in which it is difficult to obtain sufficient skin to cover the entire area, we are inclined to use pinch grafts, usually of the type suggested by Staige Davis. This type of graft will invariably grow almost uniformly, and thus hasten the epithelization of an infected field. But these grafts usually are not followed by as good cosmetic results as are the split grafts of Padgett.

When one has a clean base, and when the thickness of skin is important, the full thickness graft is ideal. This type of graft when used as a free transplant is the most difficult

to apply successfully, and, when applied, as one of the various pedicle or flap grafts, the procedure is lengthy, but the chances of success are improved. From a cosmetic standpoint the full thickness skin graft cannot be surpassed.

COMPOUND FRACTURES

Every compound fracture is potentially infected and, therefore, must be treated as though actually infected. This statement will not be questioned as regards grossly dirty wounds, but in cases of wounds with no external evidence of contamination there is disagreement from some quarters. Without being certain of the cleanliness and asepsis of the buried fragments it is too often assumed that the innocuous looking wound of the skin will heal satisfactorily and the lesion is treated as a simply fracture. The occasional wound of this type which becomes infected is responsible for the bad reputation of compound fractures. Tinker, quoted by Kennedy, stated the problem very aptly in 1909—"The most important consideration in the management of compound fractures is still the wound of the soft parts. If our wound is aseptic, tetanus and blood poisoning are impossible; bony union and a movable joint are favored; osteomyelitis will not develop; and a useful, if not perfectly normal extremity will usually be saved."

As a diversion for a few minutes perhaps you will allow me to offer two illustrations which will help to date the period to which Tinker and Kennedy make reference in the previous statement.

I was asked by the late Dr. Astley P. C. Ashhurst, during the year of the bicentennary of the introduction of Listerism into surgical technique, to determine, if possible, and to illustrate by means of graphs, the effect of asepsis and of antisepsis upon the surgical practice of the Pennsylvania Hospital in Philadelphia.

At the Pennsylvania Hospital we have continuous records of every patient from the time of its opening, in 1751, to the present. This is not even possible in the Royal Infirmary at Glasgow, where the work of Lister was first carried out. The records of his work in their wards have been destroyed.

With this type of record, and fairly constant factors, before and after statistics obtained from such a source should be of peculiar value.

Figure 12 shows the influence of antisepsis and asepsis on the number of amputations performed at the Pennsylvania Hospital before and after the introduction of Listerism. Figure 13 shows the influence of these two surgical principles on the total number of operations in the hospital during these periods.

Could a better statistical experiment be provided to demonstrate that the prophylaxis of wound infection is the prime concern of the general surgeon in the treatment of compound fractures. The best method of prophylaxis is thorough débridement before contaminating organisms establish infection which means that débridement should be performed within 6 hours after the time of injury. In a few selected cases it may be possible to débride successfully as late as 10 hours after contamination occurs but every minute saved is added insurance against infection. We must impress upon our colleagues that minutes spent in the hospital preparing for operation are just as precious as those that were spent in transportation of the patient from the site of accident to the hospital. Therefore, we should strive to organize the various hospital services so that the care of compound fractures will be given priority over that of all other operative cases.

The methods of débridement are well known, but a few remarks to emphasize certain points of technique may not be amiss.

The use of antiseptics, regardless of their innocuousness, should be confined to the skin surrounding the wound. Antiseptics should never be applied to the wound proper. Normal salt solution is the strongest solution which should be allowed to touch the exposed tissues.

Cultures of the wound, both aerobic and anaerobic, should be taken routinely at the time of the débridement if laboratory facilities exist. In addition some surgeons advocate taking smears to be examined during the course of the débridement for the immediate detection of gas bacilli.

All compound wounds should be irrigated thoroughly with normal salt solution during

and after débridement. After the final irrigation they should be dusted evenly with one of the sulfonamide powders. Recently we have used sulfanilamide for this purpose and no ill effects in the local lesion have been noted although several patients have shown rather marked toxic effects of a systemic nature. It is claimed that sulfadiazine can be administered in much larger does than any others of the group without causing toxic manifestations. It is excreted slowly and consequently we have unintentionally achieved higher concentrations in the blood than needed. In one case in which the concentration reached 21 milligrams per cent there were slight toxic symptoms which ceased when the blood level fell to 10 milligrams per cent. Whichever drug is used in the wound it should also be given by mouth as soon as the patient is able to take oral nourishment, in order to maintain the concentration in the blood at the optimum level.

On the question of wound closure we stand firmly with the conservatives. The soft tissue wounds of all compound fractures are packed wide open with vaseline gauze. Primary suture would doubtless succeed in many cases. However, because of the horrible results—osteomyelitis, amputation, or death—which may occur in wounds which become infected after primary closure, it is our opinion that it is not fair to expose the patient to a risk such as this.

Accurate reduction and complete immobilization are important. The time for reduction of compound fractures is at the time of the débridement. Most reductions can be accomplished under direct visualization and instrumental manipulation of the fragments while the soft part wound is open. There is thus no excuse for inaccurate reduction.

Fixation of compound fractures is possible by several methods.

When a nonpadded plaster casing will hold the fragments adequately this is probably the best and safest type of fixation. It introduces no foreign material into the field of operation or into the proximal or distal portions of the affected extremity. Because no special equipment or techniques are required this type of fixation is the one best suited to the occasional operator.

A more positive scheme for maintaining rigid fixation is the two pin transfixion method advocated by H. Winnett Orr. A pin or wire is driven through the proximal fragment and another through the distal fragment. By means of traction and countertraction on an orthopedic table, or on one of the special distraction apparatuses, the length and rotation of the affected bone are restored. Then while the pins or wires maintain the reduced position a plaster casing is applied which incorporates the pins or wires by means of which a more rigid fixation than can be attained with simple plaster casing is effected.

Perhaps the ideal method for maintaining reduction in compound fractures as well as in simple fractures is by means of biplane internal fixation performed simultaneously with débridement. This type of fixation must be in two planes to be effective. Frequently, the plates or screws must be removed before healing of the fracture has occurred because of infection. However, in many cases it is possible to succeed in avoiding infection as a result of the rigidity afforded by internal fixation, and the fragments will unite just as rapidly as do simple fractures which are treated in a similar manner.

We cannot leave this subject without mentioning the excellent work of Trueta in the recent Spanish War in his treatment of compound fractures by the Orr method. His monograph we recommend to every surgeon practicing in the field of traumatology. The theme which he emphasizes is that for war wounds the needs are débridement and complete rest of the tissues immediately following operation and during transportation, and infrequent dressings. The best way to afford such conditions is by means of a plaster casing. He treated 1,072 cases of open fractures of limbs by the typical Orr method. There were 6 deaths and 976 good results. This is the most convincing evidence which has as yet been offered for the excellence of this type of treatment.

CONCLUSION

In conclusion, we feel sure that most general surgeons will claim that they are fully able to provide such service as we have out-

lined, and the majority will feel that they do give such service. But do they carry this service as far as the orthopedists in their routine care of fractures? I refer to the painstaking, personal follow-up, not only in the hospital, but for months and years after the patient leaves. Is the general surgeon's aim—once a patient, always a patient? In other words, does he feel the responsibility for complete, or as nearly complete, rehabilitation as can be provided through the routine use of multiple operations, gymnastics, the swimming pool, physical therapy, and above all, occupational therapy? Is he as interested in the surgery of trauma as in that of the abdomen? If not, I am sure that patients in the future will not choose him in preference to the surgeon or an orthopedist who is. The question is not whether he *can* give the best service to such patients, but as Dr. Meeker queried, *will he?*

A CRITICAL SURVEY OF TEN YEARS' EXPERIENCE WITH FRACTURES OF THE NECK OF THE FEMUR

MATHER CLEVELAND, M.A., M.D., F.A.C.S., New York, New York

DURING the decade extending from 1930 to 1940 the fact that patients with fractures of the femoral neck may be rehabilitated in surprisingly large numbers gained wide acceptance. The enthusiasm which greeted this novel idea resulted in a vast array of techniques with relatively few careful analyses of the results attending the use of these various means of treatment.

This study of 110 fractures of the neck of the femur treated at St. Luke's Hospital during this period is an attempt to subject our experience to critical analysis and to dwell on our vicissitudes as well as our achievements. *Ad astra per aspera*, the motto of the state of Kansas, might serve as a text.

The first 50 of these patients treated during the first half of the decade have been previously reported, but they will be mentioned for contrast and to allow us to correct certain misconceptions which inexperience led us to postulate (1). These original 50 patients were treated by manipulation and application of plaster of Paris spica bandage or traction in a few instances.

In 1935 our first internal fixation of a fracture of the neck of the femur was performed. We adopted the three phlange nail devised by Smith-Petersen (4) and have never found any fixative agent to equal it. The metal used was originally stainless steel, but since 1938 we have used vitallium.

Smith-Petersen's open operative reduction and fixation of these fractures was followed in 14 patients, but the results were so disappointing that it was abandoned. It is to be hoped that other surgeons will in time publish their experiences with open reduction and internal fixation of these fractures. During this period of experimentation, we had 8 undisplaced fractures of the neck of the femur, and since we had previously satisfied ourselves that these invariably did well if they were protected, we merely kept them in bed 4 to 5 weeks and then allowed them up with a Thomas caliper splint with pelvic band and crutches. These patients have results that are in every way perfect.

Following our extremely unsatisfactory experience with open reduction, we turned in June, 1938, to closed reduction and internal fixation, and since that date 38 patients have been treated in this manner with results which are greatly improved from every standpoint.

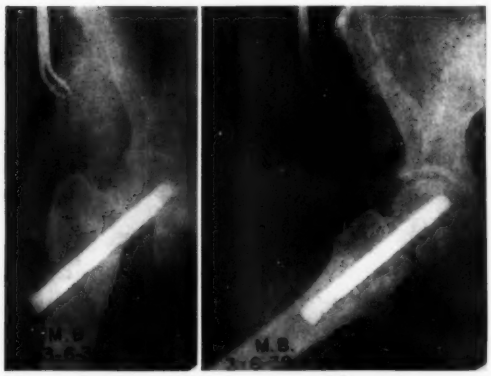
From the Orthopaedic Service of St. Luke's Hospital.
Presented in the Symposium on Fractures and Other Traumas before the Clinical Congress of the American College of Surgeons, Boston, November 3–7, 1941.

REDUCTION OF THE FRACTURE

In reporting the first 50 patients treated without surgery and in the light of a very meager experience with open reduction, the following conclusion was reached. "The chances of getting bony union with a useful hip may be greatly enhanced by open reduction, derotation of the femoral head where rotation exists, and internal fixation." This expression of opinion, backed up with but little experience, is quoted to reaffirm what now seem the important factors, namely, *reduction* of the fracture and *internal fixation*. If the fracture is reduced, such rotation of the head fragment as existed has been overcome.

The reduction of these fractures is by no means as simple as it sounds. It would seem that open reduction should guarantee the end to end apposition of the fragments, but with the instability occasioned by the dissection of the ligaments of the joint almost 50 per cent of these fractures so treated displaced during the process of nailing.

With closed reduction (3) the situation was greatly improved at once. There were 38 patients treated with closed reduction and internal fixation, and of these, 26, or 68 per cent, were practically perfectly reduced, and 6, or 16 per cent, were reduced so that the bony



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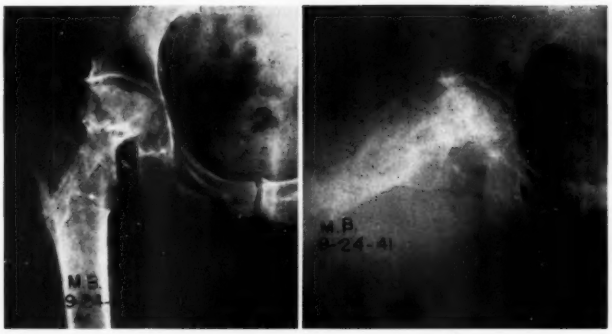


c d

Fig. 1. Closed reduction, end-to-side nailing; union with aseptic necrosis of femoral head. M. B. St. Luke's No. A 15700. Female 59 years old. Fracture of neck of right femur March 3, 1939. Reduced and nailed end-to-side shown in a and b. End-result 18 months after operation, marked aseptic necrosis of the femoral head, nail removed shown in c and d.

apposition was 75 per cent or better, and 6, or 16 per cent, of these fractures were not reduced.

Of the 26 patients who had their fractures perfectly reduced, 22 survived and all of these had their fractures united, with excellent range of motion in the hip and few if any residual symptoms. Of those 6 patients who had 75 to 80 per cent apposition of the fractured surfaces, 5 survived and united, but 2 of these showed circulatory disturbance in the femoral head and all 5 had malunion with resulting deformity.

FAILURE TO REDUCE THE FRACTURE

It seems incredible, but the fact remains that one-half of the fractures treated by open reduction were not reduced when the nail was finally driven and the operation was completed. Since closed reduction has been practiced, there have been 6 patients in 38 whose fractures have not been reduced. The reasons for these failures to secure reduction are worth recording in the 5 survivors.

1. A patient of 70 years of age whose reduction was attempted 10 weeks after injury and the fragments could not be mobilized. Nonunion resulted.

2. A patient of 70 years of age whose fracture, after repeated attempts, could not be reduced. Satisfactory roentgenograms were not obtained. Two weeks later a trochanteric osteotomy was performed, and the patient has a useful hip.

3. Two patients had their fractures "reduced" with the aid of a fluoroscope, and nailed. Check-up roentgenograms taken the next day revealed the situation that the fracture had not been reduced. This belongs in the department of locking the stable after the

a b c

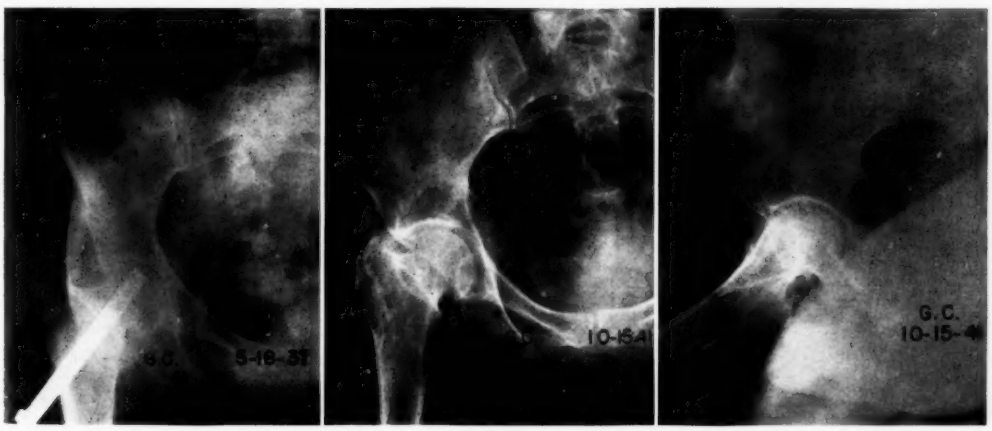
Fig. 2. Nonunion with intrusion of nail into ilium. C. B. St. Luke's No. A 27585. Female 75 years old. Fracture of neck of left femur August 19, 1939. Closed reduction and failure to reduce fracture shown in a and b. Nonunion with resulting intrusion of nail into ilium shown in c 9 months later.

horse has gone. Nonunion resulted in both. The fluoroscope serves no useful function in reduction of these fractures, and its use is not recommended.

4. In one patient, a fracture thought to be reduced with end-to-end apposition in two planes, was nailed, and a more careful study of the roentgenograms the following day showed the fragments nailed end-to-side. In this patient the fracture united, strange as it may seem, but then developed extensive aseptic necrosis of the femoral head. (Fig. 1).

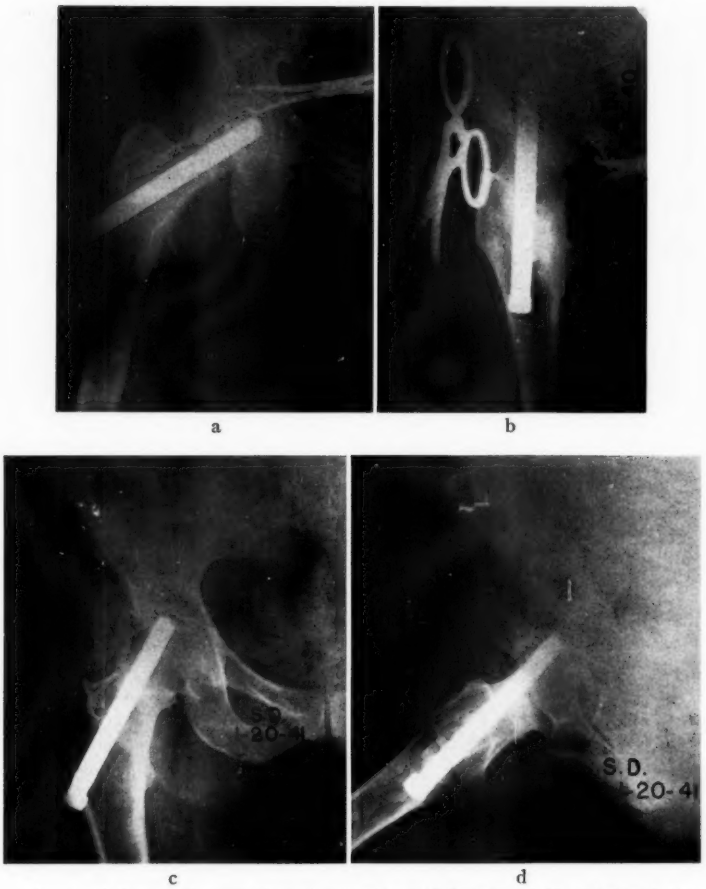
TECHNIQUE OF INTERNAL FIXATION

It is not the purpose of this presentation to deal with technique, but it may be said that the internal fixation of these fractures of the neck of the femur may be readily accomplished without the aid of any gadgets whatsoever. The proper insertion of the nail is not altogether simple, and it is only with added experience that confidence and familiarity produce uniformly satisfactory results. A nail that is centered, or practically so, in the shaft, neck, and head of the femur in both the an-



a b c

Fig. 3. Union of fracture with shortening of neck and extrusion of nail. C. C. St. Luke's No. 110-240. Female 50 years old. Fracture of neck of right femur November, 1936. Open reduction and nailing. a, Shows union with extrusion of nail 7 months after operation; b and c, end-result after 5 years, perfect except for slight shortening.



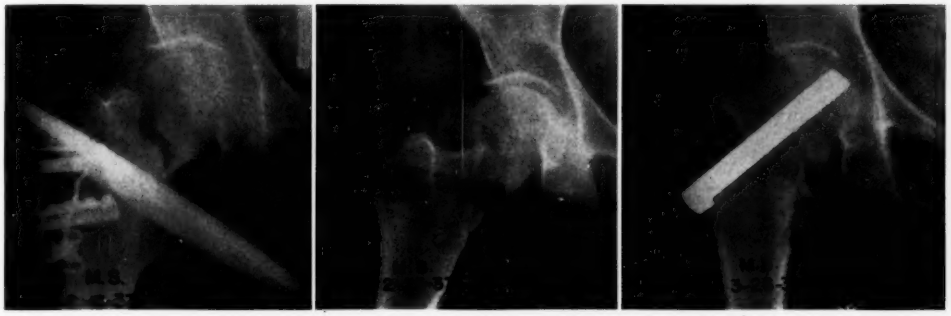
a b c d

Fig. 4. Nail overdriven at time of reduction and fixation. S. D. St. Luke's No. A 36454. Female 70 years old. Fracture of neck of right femur March 6, 1940. a and b, Show the closed reduction and the nail driven through the cartilage of the femoral head. c and d, Show the fracture united with the nail still protruding through the articular cartilage. This nail was removed. Result is excellent.

teroposterior and lateral planes, as shown by roentgenograms, is the optimum position. During the earlier years when open reduction was performed, a centered nail was placed in only 5 of the 14 patients so treated, an incidence of 35 per cent. Later, in the 38 patients treated with closed reduction an increased experience enabled us to center 21, or 55 per cent, of the nails driven. Among the entire 52 patients treated by internal fixation, there were 26 instances in which the nail was centered and 26 instances in which it was off center. Union occurred in 16 instances in which the nail was centered and in 18 instances in which the nail was off center. However, the incidence of nonunion was almost twice as frequent when the nail was off center as it was when the nail was centered.

Three phlange nail. The length of this nail varies from 3 to 4½ inches. The average patient requires a 3½ inch nail and about half of our patients had a nail this long.

The metal of which the nail was made was stainless steel, but in 1938 we changed to



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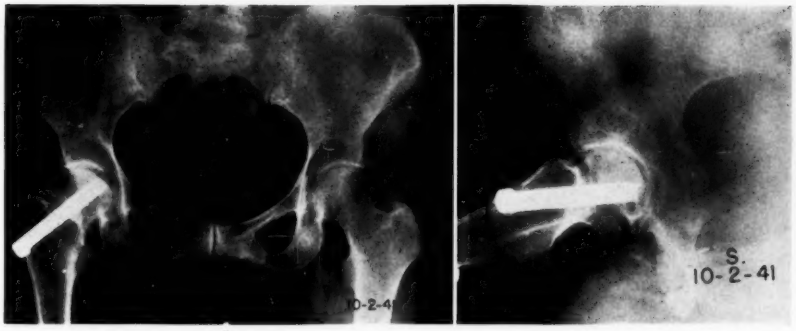

d e

Fig. 5. Open reduction, nailing, excellent result almost 5 years later. M. S. Female 68 years old. Fracture of neck of right femur February 15, 1937. a, b, and c, Show the fracture, reduction, and nailing. d and e, Show the end-result 5 years later. This is in all respects perfect.

vitallium. There has been no instance in which the nail broke.

"Migration" of the nail. There has been comment about the so called migration of the nail used for internal fixation. This occurs chiefly in instances in which there is nonunion of the fracture. In this series, there were 8 survivors with nonunion, and in none of these did the nail remain in its original position in the shaft, neck, and head of the femur. Four of these nails extruded along the original path of insertion, 2 intruded across the joint line into the ilium, 1 simply disengaged from the head, remaining loosely in the shaft and neck, while the remaining one remained engaged in the shaft and neck, bridging across a gap to the head of the femur where it was reasonably firmly seated (Fig. 2).

When the fracture is solidly united, there is seldom seen any migration of the nail. Among the 34 united fractures which were nailed, there were 4 instances in which shortening of the neck as union progressed caused an extrusion of the nail along the path of insertion (Fig. 3).

There were also 4 instances in which the nail was originally overdriven through the cartilage of the femoral head. This error is due to using a nail which is just about the same length as the shaft, neck and head pathway if driven flush and then blandly ignoring the fact that impaction of the fragments shortens the distance. When a nail of such exact length is driven fully after impaction, it is bound to penetrate the articular cartilage. There has been no further penetration of these nails (Fig. 4).

Removal of the nail. The nail has been removed only for cause. Among those patients with united fractures, 2 extruded nails, 4 over-

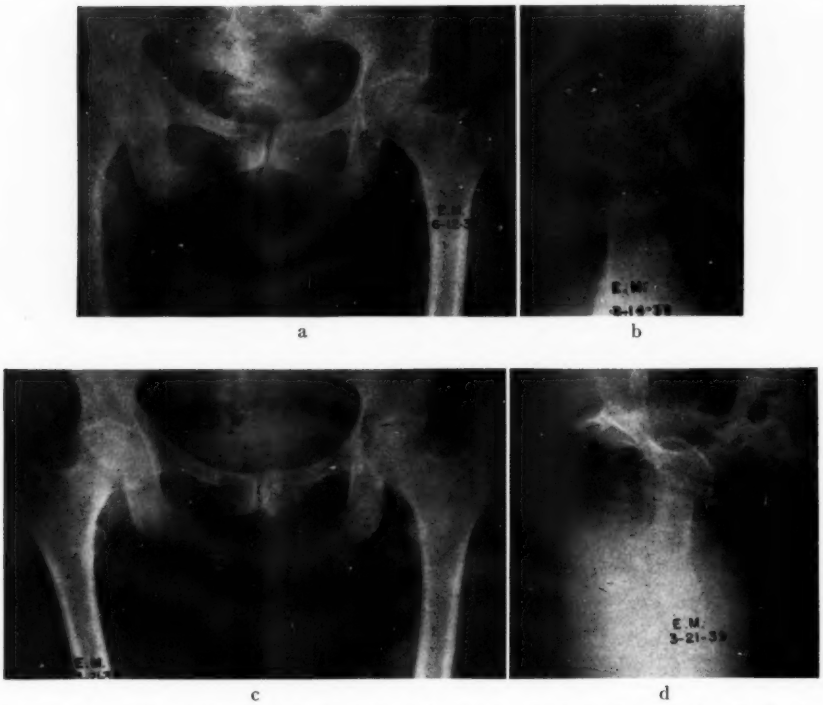

Fig. 6. An undisplaced fracture of the neck of the femur, united, excellent result. E. M. St. Luke's No. A 09391. Female 57 years old. a and b, Show fracture of neck of left femur without displacement. c and d, Show union of the fracture 9 months later.

driven nails and 5 nails in which the head of the femur showed evidence of circulatory disturbance have been withdrawn. In ununited fractures, the nail has been withdrawn in 4 of the 8 patients. In 3 of these 4 the removal preceded a trochanteric osteotomy.

Blaming the nail for failure to maintain reduction. It is our belief that instead of a certain tendency to blame the nail for failure to maintain reduction of the fracture, the responsibility should be more properly charged to the surgeon's failure to obtain an original adequate reduction.

ROENTGENOGRAMS

The paramount importance of an exact and accurate roentgen-ray technique cannot be overemphasized. The relationship of the shaft, neck, and head of the femur, and the nail must be visualized during the reduction and nailing by means of roentgenographic films taken in anteroposterior and lateral positions. With a portable roentgen-ray apparatus and a developing room adjacent to the operating room, the time of operation should be reduced to a minimum.

THE PATIENT WITH A FRACTURE OF THE HIP AS AN OPERATIVE RISK

There was but one operative death, an incidence slightly under 2 per cent. This was an elderly, hypertensive, diabetic woman who was kept in the hospital under treatment for a week prior to her operation. She died 4½ hours after operation of shock and cardiac failure.

Wound healing has, in all instances, been prompt, uncomplicated, and without infection.

These patients subjected to reduction and internal fixation have been kept in bed for 3

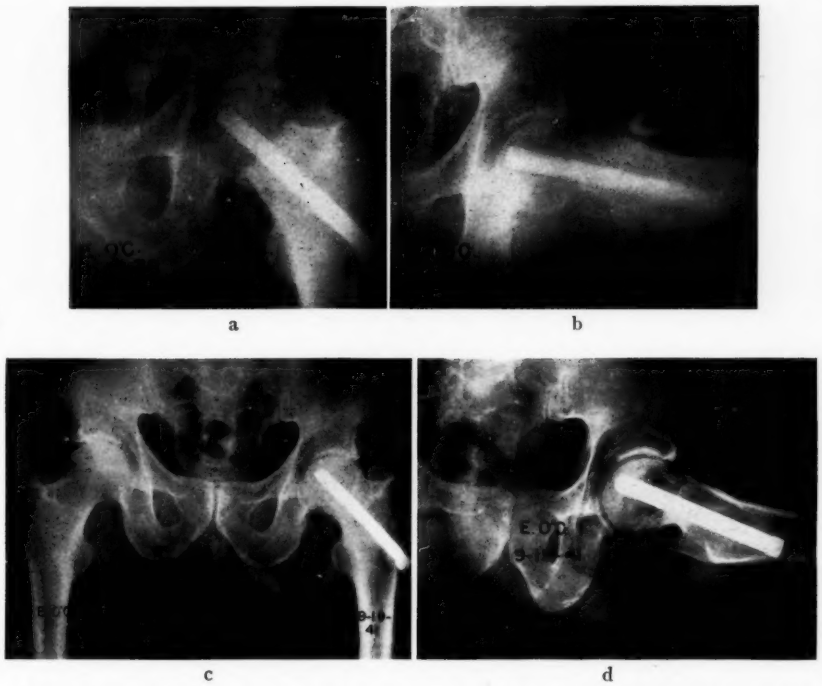

Fig. 7. Closed reduction, nailing, excellent result 3 years later. E. O'C. St. Luke's No. A 6037. Male 64 years old. Fracture of neck of left femur. a and b, Show reduction and nailing December 19, 1938. c and d, Show end-result 3 years later.

to 4 weeks after operation. Russell traction just sufficient to balance the pull of the muscles, that is, 4 to 6 pounds total, has usually been employed, and they are without pain after 2 or 3 days. Getting these elderly people with broken hips out of bed on the first, second, or third postoperative day is a stunt and serves no useful purpose. When they are allowed out of bed, a Thomas caliper splint with a pelvic band is applied and crutches are used. These supports are employed until the fracture is united or definite failure to unite is established. Union of the fracture occurs from 4 to 9 months after reduction and fixation on the average.

The average hospital stay of the 60 patients treated since 1936 has been 46 days after operation. This should be compared to an average of 122 days for the ward patients and 135 days for the private patients in our first series of 50 patients on whom no surgery was performed. The saving in time and expense to both hospital and patient is at once apparent.

FOLLOW-UP STUDY

This is an elderly group of patients, 80 per cent women, whose average age was 66½ years at the time they sustained their fracture of the femoral neck. Under ordinary circumstances there would be a considerable mortality in a similar group over a 5 year period. In the first group of 50 patients we had a 96 per cent follow-up, and in the present series of 60 patients we have a 100 per cent follow-up for an average of 23 months after the fracture for the 51 survivors. We know the end-result in every patient except one in whom sufficient time has not yet elapsed for solid union. Known 5 year results are not common, but we have 6 of them.

Mortality. During the first 5 year period there were 11 deaths among the 50 patients

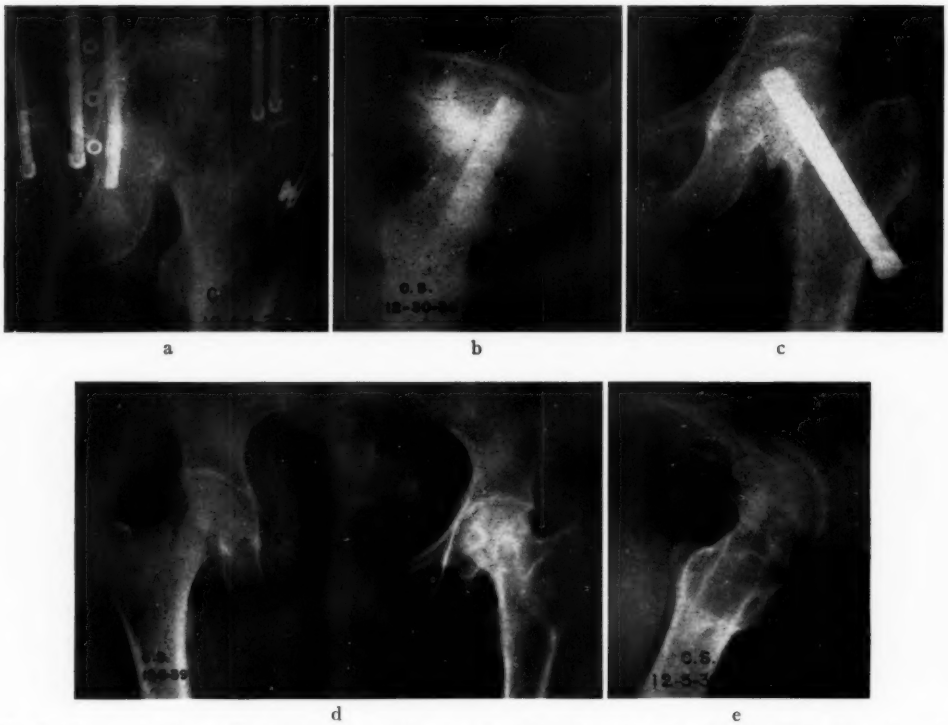

Fig. 8. Open reduction, nailing, extensive aseptic necrosis of femoral head. C. S. St. Luke's No. A 04042. Female 50 years old. Fracture of neck of left femur, open reduction. a, b and c, Show fracture, reduction, and nailing December 24, 1936. d and e, Show the end-result 3 years later after removal of nail. Some pain and limp. Patient has worn a Thomas caliper brace for almost 5 years.

treated in the main by plaster-of-Paris spica bandage, a gross mortality of 22 per cent. Four of these deaths were unrelated to the fracture, which gave a mortality of 14 per cent attributable to the fracture. Among the second 60 patients, there were 12 deaths, a 20 per cent gross mortality, with 3 deaths occurring 9 months to 3 years after the injury with the fracture solidly united in each instance. This leaves 9 deaths, or 15 per cent, as the actual mortality due to the injury. It is interesting to note, in comparing these 2 series of patients, that operative surgery neither diminished nor increased the mortality in these patients with fractures of the neck of the femur. As might be expected, those patients who died were among the more advanced in years, and 78 was their average age.

Union of the fracture. The known and widely accepted difficulty in securing union in these fractures until recently makes this subject one of absorbing interest. In the first series of 50 patients treated without surgery, union with excellent function occurred almost entirely among those patients whose fractures showed no original displacement. Only 2 patients whose fractures were reduced by manipulation showed excellent anatomical, functional, and cosmetic results.

The second series of 60 patients (52 treated surgically), whose results are herewith presented, shows a very definite trend toward the situation where union of the fracture may be interpreted as an excellent result in all respects: anatomical, functional, cosmetic.

There were 7 united fractures among the 14 treated by open reduction and nailing, but

Fig. 9a.

Fig. 9b.

Fig. 10a.

Fig. 10b.

Fig. 9. Closed reduction, union with mild condensing osteitis of femoral head. E. G. St. Luke's No. A 5569. Female 53 years old. Fracture of neck of right femur, closed reduction, and nailing October 15, 1938. a and b, Show the end-result, union with slight condensing osteitis of femoral head 18 months later. Patient is without symptoms. An excellent result 3 years after operation.

Fig. 10. Nonunion of fracture treated by trochanteric osteotomy. M. D. St. Luke's No. A36710. Female 70 years old. Fracture of neck of right femur unreduced. a, Shows the unreduced fracture, extrusion of nail. b, Shows trochanteric osteotomy united, head of femur still ununited to neck. A useful weight-bearing mechanism.

only 2 of these, or 28 per cent, of those united were excellent results (Fig. 5). The 8 undisplaced fractures treated without surgery were all excellent results from every standpoint (Fig. 6). Among those patients treated by closed reduction and nailing there were 27 whose fractures united and 24 of these, or 88 per cent, of those united were excellent in every respect (Fig. 7) while the 3 others had deformity due to malunion or varying degrees of circulatory disturbance in the femoral head sufficient to cause some symptoms.

A comparison of the incidence of union in the two series of cases and of the various methods of treatment in the second series is shown in Table I.

To make a long story very short indeed, union of fracture of the neck of the femur, in our hands, increased from 47 per cent of the survivors in the first half decade to 83 per cent of the survivors in the second half decade. The credit for this must be ascribed to internal fixation and increasingly improved reduction of these fractures.

Circulatory disturbance in the femoral head. The recently completed study by the Fracture Committee of the American Academy of Orthopaedic Surgeons (2) speaks of the incidence and degree of arthritic changes in the femoral head encountered in these fractures. The term arthritic changes is misleading, and I believe circulatory disturbance or change is

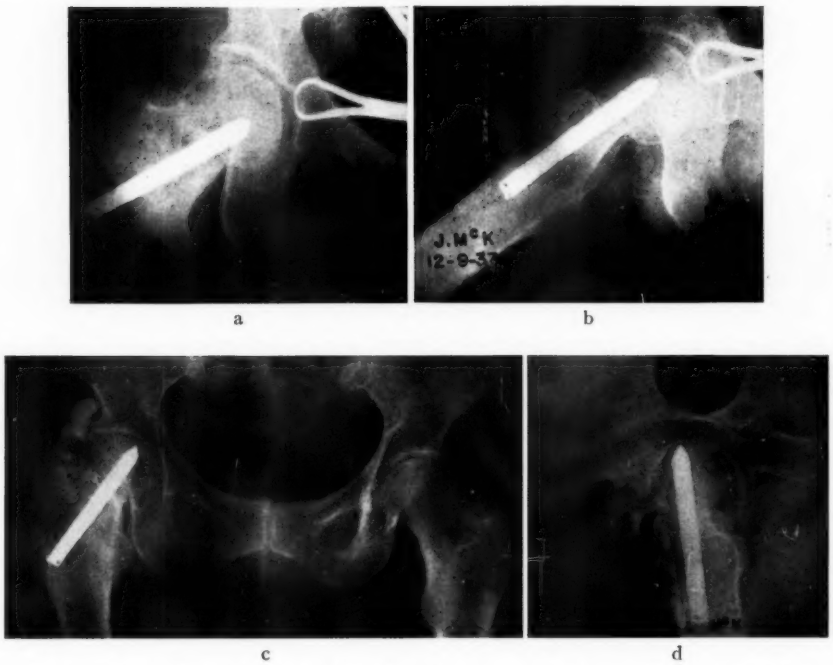

Fig. 11. Open reduction, malunion with bizarre bony overgrowths from the acetabular margin. J. McK. St. Luke's No. A 03598. Female 67 years old. Fracture of neck of right femur December 7, 1937. a and b, Show fracture and incomplete reduction. c and d, Show malunion with bony overgrowths from the margin of acetabulum 18 months after operation. This patient had a useful and symptomless hip when last seen 2 years after operation.

preferable because arthritis of the hip is known and recognized in its various forms, while the alteration of the femoral head due to interference with its blood circulation is a different picture.

Actual arthritic change involving the hip joint following a fracture of the neck of the femur was found only once in this series of 60 patients.

These circulatory disturbances or changes in the femoral head may vary from a mild condensing osteitis to an advance aseptic necrosis. In our experience, they have invariably appeared within the first year after the fracture. We have had no instance in which the circulation failed after the first year had passed and union of the fracture was established.

The greatest predisposing cause of circulatory disturbance in the femoral head is nonunion of the fracture. Six of the 8 patients with nonunion showed extensive aseptic necrosis of the femoral head.

Of the 7 patients subjected to open reduction of their fractures which united, 3 had extensive aseptic necrosis of the femoral head, an incidence of 42.8 per cent (Fig. 8).

Among the 27 patients with union of their fractures treated by closed reduction and internal fixation, 4 had a very slight condensing osteitis (Fig. 9), and 1 had an advanced aseptic necrosis. Three of these 5 patients had incompletely reduced fractures. Of the 8 patients with undisplaced fractures treated without surgery, none showed the slightest evidence of circulatory disturbance, but 1 patient with an undisplaced fracture which was nailed showed definite circulatory disturbance.

One is forced to the conclusion, in this series of patients, that the most important

TABLE I.—INCIDENCE OF UNION AND NONUNION

Series 1. 1930–1935 Nonoperative	Total in group	Union		Nonunion	
		No.	Per cent	No.	Per cent
Known	48	19	39	29	61
Living	38	18	47.4	20	52.6
Dead	10	1	10	9	90
Series 2. 1936–1941 52 patients operated upon and 8 undisplaced fractures not operated upon					
A. Open reduction and internal fixation					
Known	14	7	50	7	50
Living	10	6	60	4	40
Dead	4	1	25	3	75
B. Undisplaced fractures nonoperative					
Known	8	8	100	0	0
Living	8	8	100	0	0
Dead	0	0	0	0	0
C. Closed reduction and internal fixation					
Known	37	27	73	10	27
Living	29	25	86	4	14
Dead	8	2	25	6	75
D. Entire second series					
Known	59	42	71	17	29
Living	47	39	83	8	17
Dead	12	3	25	9	75

cause of circulatory disturbance in the femoral head has been failure to reduce the fracture and keep it reduced. For the benefit of those who feel that circulatory disturbance is more

TABLE II.—INCIDENCE OF CIRCULATORY DISTURBANCE IN THE FEMORAL HEAD

	Total	Mild condensing osteitis of the femoral head		Aseptic necrosis of the femoral head	
		No	Per cent	No	Per cent
Patients with nonunion	8	0	0	6	75
Patients subjected to open reduction and nailing. United	7	0	0	3	42.8
Patients subjected to closed reduction and nailing. United	27	4	14.8	1	3.7
Patients with undisplaced fractures not operated upon	8	0	0	0	0
Total united fractures	42	4	9.5	4	9.5

frequent in the younger age groups, it may be stated that the average age of the 8 patients who showed this phenomenon together with union of the fracture was 62 years, 4½ years under the group average. Those 6 patients with ununited fractures who showed marked circulatory disturbance in the femoral head were 70 years of age on the average. The circulatory changes encountered among those patients may be summarized as follows, in order of frequency of occurrence.

NONUNION OF THE FRACTURE

This is a problem which is definitely diminishing but will doubtless continue to exist. The situation of these patients can be greatly alleviated as far as pain and instability are concerned by a trochanteric osteotomy of the femur. This operation has been performed on 3 of our 8 patients with ununited fractures with great improvement in their situation (Fig. 10).

SUMMARY

Open reduction and internal fixation. In our hands, open reduction and internal fixation of these fractures of the neck of the femur offered very little improvement in end-results over those obtained by nonoperative means. Of the 7 patients whose fractures united, only 2 were wholly satisfactory. There were 3 cases of extensive aseptic necrosis and 2 bad malunions with marked deformity. In certain cases of open reduction, there occurred bizarre overgrowths from the acetabular margin, perhaps due to stripping of the periosteum (Fig. 11).

Undisplaced fractures. During this period of tribulation in dealing with open reductions, the undisplaced fracture of the neck of the femur, treated by 3 to 4 weeks' rest in bed and weight-bearing after the application of a Thomas caliper brace, gave invariably optimum results. Since our nailing technique has improved, a number of these undisplaced fractures have been nailed without reduction.

Closed reduction and internal fixation. The accurate reduction by manipulation and the careful insertion of a three phlange nail has yielded surprisingly good results, union of the fracture in 86 per cent of the survivors. We make every effort to center the nail in two planes but are not always successful. Overdriving the nail through the articular cartilage of the femur has been done in 4 instances. It is due to carelessness and can readily be avoided.

Circulatory disturbance in the femoral head. The circulatory disturbance in the femoral head, based on our experience with these 60 patients, has always appeared within the first year after the fracture. Seventy-five per cent of the patients with nonunion of their fractures had extensive circulatory disturbance in the femoral head. Of those subjected to open reduction with their fractures united, 42.8 per cent showed extensive aseptic necrosis of the femoral head. Of those 27 patients with united fractures who were treated by closed reduction and nailing, 18.5 per cent showed some evidence of circulatory disturbance, for the most part very mild. The majority of all patients showing circulatory disturbance in the femoral head with fractures united had inadequate reduction of the fracture.

Adequate reduction of the fracture. We have found in this series of 60 patients that accurate reduction of the fracture is the most important single factor in securing union and avoiding circulatory disturbance in the femoral head. The actual or so called migration of the nail is usually due to failure to properly reduce the fracture, and this migration occurs almost exclusively in ununited fractures.

Nonunion. Patients with nonunion of their fractures may be greatly benefited by a trochanteric osteotomy of the femur.

CONCLUSION

An accurate end-to-end reduction of a fractured neck of the femur by manipulation and fixed by a properly placed three-phlange nail should result in a very high percentage of unions, 86 per cent of the survivors in this series, and a low incidence of circulatory disturbance in the femoral head. This procedure is, therefore, recommended.

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FACTORS IN THE CHOICE OF MATERIAL FOR BONE PLATES AND SCREWS

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THE qualifications for determining and specifying the basic factors that are essential in internal fixation of fractures with metals should be defined. As I see it there are three cardinal principles, three essential factors, which must be accepted and considered as a whole for the single purpose of securing and maintaining fixation without incurring changes that are detrimental to bone and that thus defeat the purpose of mechanical stability. These factors are: (1) electrolysis (chemical); (2) physical properties; and (3) application.

ELECTROLYTIC (CHEMICAL) FACTOR

The entire change in our attitude and thought lies in the basic principle involved in the electrolytic factor. Without recognition of potential chemical changes resulting from the use of material affected by body fluids as the cause of deleterious effect upon bone, no matter how strong or how well applied the instrument used, a large percentage of delayed unions, nonunions, and marked bone necrosis as result of local decalcification and even osteomyelitis may be expected to occur.

I am aware that to delve at this time into all the whys and wherefores of electrolysis, the passing of electrons between metals of different potentials of electromotive force set in action by an electrolyte, and the series of changes that occur, would not only bore you, but defeat the purpose of bringing about the broader understanding of the principle I desire to express, so I shall try not to be too technical.

Practically all of the so called metals we use are a composite of different basic elements, each having a potential of different electromotive force, and are known as alloys. They offer varying qualities of resistance to the given fluid to which they may be subjected; some are more resistant to acids, others to alkalies, but in the variance of the degree of resistance electrons pass from one element to the other. Thus the atoms of one constituent are combined with or separated from those of the other through the mobilization of ions which is electrolytic action. When any alloy, generally referred to as a metal, is spoken of as being passive in a given fluid it is meant that that metal is so resistant to that electrolyte (fluid) that the passage of electrons is reduced to such a minimum that corrosion is practically nonexistent.

When plain iron nails were used in fractures (which is within my memory) they caused little trouble, but when metallurgists began to make steel out of iron by adding elements to it, our trouble began. After our first announcement of the result of a series of experiments in determination of the part electrolytic action had to play, an unfortunate statement was made in error on a similar occasion that "all the changes in bone resulting from the use of metals in fractures ascribed to electrolysis were simple oxidation and were not the cause of loosened screws, or the discoloration of tissue, or excess of serous fluid, about the plates and screws," and unfortunately it apparently created a great deal of confusion.

When electrons are removed from an ion, atom, or molecule, the substance is oxidized; when electrons are added to a substance, it is reduced. Thus, every electrochemical change which takes place involves both oxidation and reduction.

If the difference is understood between one pure metal which is not subject to corrosion and a multiplicity of different metals combined into one (an alloy) which is subject to corrosion, then it is clear why a single screw or plate—unless it be of a single element—is no longer a single metal and why it will corrode unless made resistant to the fluid to which it is to be exposed.

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I desire further to emphasize the point that different materials used in conjunction with each other, such as the combination of passivated stainless steel screws in a vitallium plate, etc., only serve to make stronger and more destructive batteries, though each may be inert if used separately. Only properly passivated steel should be used throughout, or vitallium or tantalum should be used throughout. A combination of materials should never be used. An order to this effect has been issued to all Army hospitals by the Surgeon General of the Army.

It must be further understood that metals for use in surgery are passivated to be resistant only to blood serum or normal salt. For instance, 18-8 steel with molybdenum is resistant to solutions of sodium chloride but less resistant to bromium chloride, and not at all to iodine chloride; therefore, the use of other chemicals in a wound, especially iodine in conjunction with metal fixation, should be carefully avoided.

There are two recent articles in which use of Dakin's solution (hyperchlorite of soda) is advocated in the treatment of infected wounds in which compound fractures are plated to maintain fixation. Hyperchlorite of soda is a much stronger electrolyte than salt solution and may energize electrons not only in the substance of the plate but throughout the screws and so initiate destructive bone changes about the latter thereby causing an osteomyelitis otherwise avoidable.

Today there is increased interest and effort by metallurgists to create alloys that are as resistant to corrosion as possible for many industries as well as for bone surgery, but the criterion of that resistance which we must understand and demand must be all the more carefully assayed for our use.

The manufacture of alloys is one of the most intricate of technical specialties. It is not so simple as having a formula, just placing the materials in a oven, and creating steel. Moreover, because of the complexity of manufacture, each batch turned out must be carefully tested to meet specifications and required standards.

We now have as a guide the basic principle that material must be sufficiently inert in the body through its chemical resistance to the electrolytic effect of body fluids to remain so. Through clinical experience and observation over sufficient time we have come to expect and to realize the necessity for the inclusion of this factor in any attempt to standardize the material to meet our requirements.

The Subcommittee on Education of the Committee on Fractures and Other Traumas of the American College of Surgeons, consisting of Drs. Huber Wagner, Clay Murray, and me, is now actively engaged with metallurgists and the Bureau of Standards at Washington in the creation of such standards as are essential to meet our needs, based upon the practical absence of electrolytic changes and of assured physical stability. The minimum requirements established are to be based upon results of tests of such materials as have been found to remain passive in experimental animals and in clinical cases for 2 or more years and upon tests of their physical fitness to withstand the stress and strain entailed. It is up to the metallurgists to create such materials from available materials to meet these required standards.

PHYSICAL FACTOR

There is much more to the detail of the requirements of physical fitness than shape and size; so that, though articles of different design may be added from time to time, all must conform to necessary specifications as to strength, ductility, malleability, fragility, torsion, and resistance to fatigue as well as resistance to corrosion which has been described.

The crucial failure of our previous effort to standardize plates and screws was to allow any manufacturer to produce them according to the formula sanctioned by the Bureau of Standards. The result was that vanadium steel plates appeared on the market with as many different characteristics and sold at as many different prices as women's hats.

The degree of heat applied in preparing the different metals to be combined, the difference in heat during the process, the manner and speed at which they are cooled, the way in which they are mixed, as well as the selection of elements for use and the proportions, control the properties of the finished product.

Whether such metals are finished by machine or are cast, and whether or not the constituents are free from impurities, are factors which govern the price. Cheap, impure metal is the bargain stuff of the itinerant salesman. Is not success in attaining union of a fractured tibia worth more than the small difference in the cost of a plate?

The committee in its protocol of standards is not interested in low cost, or is it trying to meet prices. It is proceeding on the basic assumption that the surgeon desires only articles that will aid in the attainment of his goal and furthermore desires to be protected from unreliable gadgets.

The Pure Food and Drug Act protects us from impure chemical products. It is just as important, since we know what chemical and physical properties are essential for safety, that our patients and we be protected from metals that are unfit and may cause harm.

In addition to passivity, however, and to rigidity and strength it is most important that materials have varying properties; some must have machinability, others ductility and tensile strength so that the finest wires may be produced from them. In passing I will say that it is just as important for the abdominal surgeon to have passive material for wire sutures to bury in the tissue, though changes are not as obvious in abdominal surgery, as for the bone surgeon who uses the nail, even though the latter has the additional hazard of calcium changes due to electrolysis—splendidly termed by Masmonteil "electrolytic ostiitis."

APPLICATION

While chemical and physical properties of plates and screws can be made to conform to minimum standards, their application in surgery cannot be controlled. Surgical judgment cannot be accurately measured nor technical skill standardized. Instead we can only point out principles for the application of plates and screws which will facilitate their use and will be most likely to ensure success.

Plates must be selected which are of sufficient strength and size to hold the involved bone. Small, short narrow plates, it goes without saying, are inadequate for immobilizing a fractured femur in a large adult. Before the electrolytic factor was recognized in its effect in the decalcification of bone, plates, such as the Sherman type, were made in order to minimize the volume of material, for it was recognized that the deleterious effect of metals seemed to be in proportion to the extent of metallic contact. Now we know that plates may be as wide or as heavy as necessary to meet the requirements of stable fixation. I think that the length of the plate should be at least three times the diameter of the bone involved to provide proper lever support. Moreover, the plate should be shifted about or bent until it conforms closely to the surface of the bone so that a tight grip may be obtained. Whether the plate is thick, or thin, wide or narrow, straight or curved, is unimportant so long as it fits snugly and is sufficiently strong to support the bone ends involved. It should be malleable enough to be bent and still tough enough to meet the strain required.

A single screw on either end of a plate beyond the fracture should never be used as it creates a hinge at the fracture site. Also a plate applied with two screws on one side of a fracture and only one screw on the other side is bad mechanics.

The drill holes for the screws should be about the same diameter as the shank of the screws. A drill slightly larger than the shank makes a hole in which the threads are insecurely anchored and likely to strip out of the bone. A drill slightly smaller makes a hole in which the screws cannot be inserted without great force. As a result, screw drivers slip, screws break, tempers are lost, and the whole operation may be ruined.

An exception to this rule is that a drill must be smaller than the shank of the screw when it is to be inserted in atrophic or decalcified bone. Obviously, in soft bone in which it is difficult to secure any sort of hold with a screw, the chances of success are greater when the screws compress the cancellous bone into a more firmly compact media. Conversely, the drill should be larger in very hard or eburnated bone.

The choice of the type of screw to use is easily made if several important points are borne in mind. In the first place, long screws obtain a more secure mechanical grip on the

a b c

Fig. 1. Types of screws: a, dowel, b, wood-plain, c, wood-pull up. Note the obliquity and wider thread of the wood type screws.

bone than short screws, and engagement of both cortices of the bone is more likely to prevent motion of the fracture than if only one cortex is secured. Holes drilled entirely through the bone permit the ends of the screws to penetrate the opposite cortex and hold the plate firmly without impeding the tightening of the screws.

Whether one uses a Sherman type of screw with its dowel end that is supposed to drill its way or a machine type of screw rather than a more deeply threaded wood type is immaterial so long as a tight grip is obtained. I personally prefer the last as it seems to obtain better engagement and is easier to apply. Any of these types are applicable to plates in which the detail of counter sinking or special screw heads are subjects of choice.

There is, however, another type of screw (Fig. 1) which is important. This is the wood or "pull up" type of screw which has a smooth shank of the diameter of the thread between it and the head of sufficient length to reach through the proximal cortex. The reason for this is that when the threads have pierced the opposite cortex the distal fragment is drawn tightly against the proximal fragment as the shank turns freely in the proximal cortex with the head against the bone as a fulcrum. A larger drill hole proximally serves the same purpose. On the other hand if threads are engaged in the proximal cortex the opposite fragment will be pushed away no matter how tightly the head may be against the bone. All carpenters know this when they wish to fasten boards tightly together.

After screws and plate are applied to the bone it is essential that adequate support and fixation of the extremity be provided as it is fallacious to assume that a plate alone, no matter how strong, will hold the fracture ends tightly enough together to permit early exercise unless both peripheries are fixed. While the plate holds the upper periphery together, during extension the margins of the opposite periphery are pulled apart. To illustrate: if solid plates be substituted for hinges on a door it takes little force to show a crack on the opposite side. So in cases in which but one side is fixed with a plate alone, a plaster cast controlling proximal and distal joints is necessary (Fig. 2).

This problem is encountered particularly in transverse or short oblique fractures of the femur and tibia due to the recumbent posture of the convalescent patient in whom it is so essential to maintain knee and ankle function, especially the former in which function is so easily lost. Because of the weight of the leg and the sag in the thigh or leg downward from the point of suspension by the plate on the upper periphery, the margins of the lower periphery are separated in an inverted V throughout the width of the fracture ends. This is true no matter what manner of external fixation or support is used or how rigid the plate may be due to laxity of the posterior muscles which are beyond control of external fixation. Such a gap naturally predisposes to delayed union or to nonunion.

To meet this condition and secure an equally rigid fixation of both peripheries, a long screw of the pull up or wood screw type, placed obliquely to the axis of the plate through the upper surface of the proximal fragment, downward and backward across the fracture site, through the cortex of the distal fragment, will draw the fracture ends tightly together at the periphery opposite the plate and at the same time prevent any tendency to rotation of either fragment and also will materially lessen lateral movement (Fig. 3). This does not mean, however, that no external support is necessary, that the limb is turned loose, and the patient permitted to get up and walk. After suture of an abdominal wound, the patient is kept in bed a reasonable time for wound healing, and so for bone healing there must be additional proper support and time allowance. However, stable fixation allows almost immediate hip, knee, and ankle function. In other words, encasement of the limb in plaster may and should

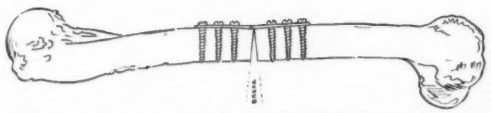

Fig. 2. "Sag separation" of the periphery distal to the plate resulting from fixation with a plate on but one side of the bone.

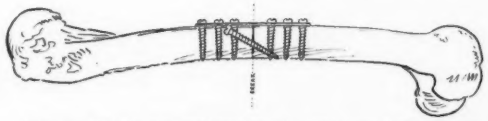

Fig. 3. Stable approximation of distal periphery by engagement with transfixion screw placed obliquely through both fragments.

be avoided if possible, while a plaster gutter with suspension in a Thomas half ring splint with the knee joint usually is quite sufficient. Such a procedure may be expected to shorten the period of disability to some 6 to 10 weeks as compared with the 12 to 20 weeks usually allotted.

The long oblique fracture offers yet another problem which, however, is more easily met through control of the distal periphery by complete transfixion of both cortices transversely by the use of pull up or wood type screws to draw the fragments together tightly. Two or more such screws may be so spaced that the fractured surfaces are held so firmly that joint function is admissible directly. In such instances, the addition of a plate is rarely necessary unless there is a complicating transverse fracture in the same field.

In short, bone as other tissue must be closely approximated and held so that it may regenerate promptly in the process of new cell growth. This emphasizes the essential in plating that close approximation of the bone ends must be obtained in all instances whether additional transfixion screws are applied or not. We see far too many cases of delayed union or nonunions because of improper application of a plate in which a gap of a 1/32 or 1/16 inch or more has been left.

My theme, however, is in principle, so details of varied technical applications of plates and screws will not be discussed. As I see it, the most important principle evolved is the chemical factor through the understanding of which it now becomes possible to apply direct fixation to fractures under conditions heretofore impossible. Compound fractures occurring in the presence of most severe trauma and infection with the outlook of bone union during the period of healing of an infected and traumatized wound may be expected in a very high percentage of cases. In many instances it is possible now to plate and close a compound fracture after proper débridement and to expect wound healing as well as bone union as though a simple fracture were present.

During the past war direct fixation was forbidden because metals we then had were highly electroactive and increased the damage through deleterious bone changes so that nonunion and even amputation resulted. Today we can feel safe in using metals for we now have available material that is passive; this fact has been proved in the recent past in the most severely traumatized and infected compound fractures occurring in the toll of automobile and airplane accidents as well as in industrial surgery. The same expectancy of greatly diminished nonunions and even amputations may now be expected in compound fractures occurring in war wounds.

SUMMARY

The first two factors, chemical and physical fitness, in the material for use in the treatment of fractures are supplied us by metallurgists; the third factor, application, must be mastered by each of us individually by an understanding of the mechanical principles involved, skillful technique, and that judgment acquired only through training and experience.

The introduction into bone surgery of material that is so tolerated as to cause no disturbance, opens fields we have not before known; but we must warn that it becomes a dangerous tool in the hands of those not qualified to use it. The same hesitancy and respect should be felt in operating to reduce fractures as in performing gastrectomies or in operating upon the brain. I say this because I believe that though the first two factors which have been mentioned are essential, the last—application—is the *sina qua non* of success.

RESULTS IN COMPOUND FRACTURES WITH OSTEOMYELITIS AS EXPERIENCED BY THE VETERANS ADMINISTRATION OVER THE PAST TWENTY YEARS

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IN modern warfare low velocity missiles cause the majority of compound fractures with their associated lacerations and contusions contaminated by clothing and skin, resulting in gross infection after about 12 hours.

The standard treatment during and subsequent to the last war for compound fractures and osteomyelitis, according to the Surgeon General's Report of the Army for 1927, was as follows: (a) proper splinting for transportation and first aid; (b) débridement; (c) skeletal traction and/or other immobilization; (d) Carrell-Dakin treatment or dichloramine T.; (e) surgery other than débridement as indicated; (f) amputation and plastic repair; (g) physical therapy.

During the fiscal year of 1926, a summary of fractures and amputations of the long bones was studied by the Veterans Administration. The greatest number of fractures, 4,736, occurred in the humerus; the next greatest in the femur. The greatest number of deaths, 1,060, or 35.03 per cent, resulted from fractures of the femur.

The tables covered a study of 22,954 fractures of the long bones over a period of 6 years. This group formed 5 per cent of the World War Veterans disabled to a compensable degree. The rating schedule used throughout the period under study based the degree of disability upon the average impairment of earning capacity resulting from injuries in civil occupations. On that date, 15,597 or 54 per cent of the fractures had reached a stationary level, which was reasonably certain to continue throughout the claimant's life. Thirty-nine per cent of the total showed improvement and 7 per cent had retrogressed.

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Fractures of the femur comprise the group of most serious injuries in the length of time required to reach a stationary level and in the high degree of disability. Amputation of the

TABLE I.—SURGEON GENERAL'S REPORT, 1927

	No. cases	Per cent	No. days
Fractures following gunshot wounds—61% returned to U. S. for treatment...	25,272		
80.31% compound.....	6,006		
Fractures, nonbattle, due to injuries, simple.....	39,569		
Total.....	70,847		
Percentage of injuries caused by low velocity missiles..		70.41	
Loss of one or more extremities.....	4,403		
Associated joint involvement (ankylosis, flail joints, contractures, etc.).....	4,970		
Percentage of total discharges for disability due to fractures.....	11,740	46.6	
Days lost due to fractures...			5,125,220
Per cent of all days lost due to all causes.....		29.3	
Average duration of treatment			225.50
Percentage of deaths as result of fractures in comparison to total.....		20.0	
No. deaths from fractures....	2,757		
Total No. deaths.....	12,470		

TABLE II.—STUDY OF END-RESULTS IN FRACTURES OF LONG BONES BY THE U. S. PUBLIC HEALTH SERVICE AND U. S. VETERANS ADMINISTRATION, 1919–1926

	No. cases	Per cent
Simple fractures.....	4,519	16.69
Per cent under 30 years old.....		69.05
Per cent stationary.....		54.
Per cent improved.....		39.
Per cent retrogressive.....		7.
Compound fractures.....	18,435	80.31
Complications—		
Osteomyelitis.....	4,053	
Ankylosis, shortening, deformity, nonunion, faulty union, nerve involvement, etc.....	10,505	
Total.....	14,558*	

*4,244 of these had ratings of total permanent; 1,362 of less than 10%

TABLE III.—STUDY OF END-RESULTS IN FRACTURES OF LONG BONES BY THE U. S. PUBLIC HEALTH SERVICE AND U. S. VETERANS ADMINISTRATION, 1919–1926

	No. cases	Per cent	Years to become stationary	Per cent	Amputations	Less than 10 per cent	10–29 per cent	30–49 per cent	50–79 per cent	80–100 per cent
Femur	5,138	23	4 or more	71	1,738	270	1,673	726	1,671	808
			5+	51						
Tibia and fibula	4,485	20	4	13	1,140	764	1,968	1,272	244	216
			5	23						
			5+	49						
Humerus	4,328	19	4	11	1,183	416	1,752	734	637	709
			5	22						
			5+	55						
Radius and ulna	2,340	10	4	13	521	399	1,003	204	581	63
			5	23						
			5+	49						

thigh contributed largely to the high rate of disability. Table IV and the amputation report, by specific bone or bones, show the interval elapsing between the injury and the amputation. Of the 4,179 amputations, 3,044 or 73 per cent were done within the first 15 days after injury. The United States thus profited by the experience of the French and British by having mobile hospitals sufficiently equipped with surgeons and instruments to perform major surgery within the first 72 hours after injury.

It should be noted that the average period of disablement is greatly in excess of the period recorded by observers for industrial fractures. This is because the greater number of these fractures were compounded due to severe battle injuries. Many of them later became septic with much destruction of tissue, including osteomyelitis, resulting in lasting deformity and much impairment of function. Therefore, the character of these fractures is of a far different type from those of civil life so the final results are not comparable.

TABLE IV.—STUDY OF END-RESULTS IN FRACTURES OF LONG BONES BY THE U. S. PUBLIC HEALTH SERVICE AND U. S. VETERANS ADMINISTRATION, 1919–1926

AMPUTATIONS

Interval elapsing between injury and amputation	Days 1–31	Months 2–48	Over 4 years	Death	Total
Thigh	1,374	354	14	76	1,818
Leg	860	256	25	49	1,190
Arm	641	44	3	39	727
Forearm	391	27	3	23	444
Total	3,266	681	45	187	4,179

AMPUTATION REPORT

Phalangeometatarsal and transmetatarsal amputations. These were infrequent but amputations in this area gave good function.

Lisfranc's amputations at the transmetatarsal joint gave reasonably good function. The dorsal flexors should be anchored to the ends of the bones to preserve dorsal flexion.

Transtarsal amputations. Distal to Chopart's joint was preferable to Chopart's amputation, as proper balance of the dorsal and plantar flexors of the foot was better preserved.

Chopart's amputations resulted in poor function. Plastic repair did not usually improve the function and reamputation was often necessary. Equinus deformity frequently developed and the stump was too short for proper prosthesis.

Pirogoff's amputation. Displacement of the remaining portion of the calcaneus was common. The total end bearing stump, following the Syme's amputation, is quite as satisfactory.

Syme's amputation. The chief advantages in the Syme amputation were that it was total end bearing and the length of the limb was approximately preserved so the patient could get about without his prosthesis. This amputation has been found highly satisfactory and must be considered as a site of election.

Leg, lower third. All cases observed required reamputation because of poor vascularity and complications.

Amputation of leg (calf) was considered in the Surgeon General's Report, 1927, as the ideal site for anatomical and prosthetic reasons. Subsequent experience in the Veterans Administration has shown a high percentage of neuroms, ulcers, painful stumps, and painful weight bearing surfaces. Reamputation (Gritti-Stokes or thigh) has been found the only answer to the problem in many of these cases.

Thigh. Knee joint and transcondylar amputations were found unsatisfactory. Gritti-Stokes amputations required a high percentage of reamputations (Surgeon General's Report, 1927). Subsequent experience points with favor to this operation provided the patella has firmly adhered to the femur and is well placed. Amputations at various levels from high transcondylar to 2 inches below the lesser trochanter have proved satisfactory. Amputation through the neck of the femur has been found preferable to disarticulation at the hip joint.

Hand. Cases in which only a débridement with heroic efforts to save all tissue possible, pedicle transplants, and plastic repairs offered the most desirable results. Transcarpal amputation was found preferable to amputation at the wrist. Wrist joint amputation was preferable to any higher up. The club-like stump eliminated much apparatus in the prosthetic hand.

Forearm. Amputation in the forearm should be done as low as possible. The importance of preserving supination and pronation warrants careful treatment of the periosteum to prevent bridging. A forearm stump should not be sacrificed to overcome painful scars, ulcers, etc., but plastic measures should be used on the soft structures.

Arm. Transarticular and transcondylar amputations have not proved satisfactory from the standpoint of prosthesis. Above this level all possible bone length should be saved. Short arm stumps may be improved so far as leverage is concerned by severing or raising the insertions of the pectoralis muscles, the latissimus dorsi, and teres major. The head of the humerus should always be saved if possible, to preserve the contour of the shoulder.

CONCLUSIONS

1. Eighty and thirty-one hundredths per cent of battle fractures were compound; nearly one-half of all discharges, nearly one-third of all days lost and one-fifth of all deaths were the result of fractures.

2. About one-half of all compound fractures required more than 5 years before becoming stationary.

3. The relatively large number of late amputations indicates early surgery is advisable and that mobile hospitals should be equipped for major surgery.

4. Seven years after World War I the majority of compound fracture cases were compensable from 10 per cent to 50 per cent, with a smaller but still large number from 50 per cent to 100 per cent.

5. In 1930, there were about 10,000 old and recent cases of osteomyelitis in the Veterans Administration due to all causes. From the treatment of these cases, the following conclusions may be drawn:

a. In cases of compound fractures early anatomical alinement should be accomplished by open or closed manipulation with maintenance by external or internal fixation. Hardware, such as Parham bands, Lane or Sherman plates, screws, etc., may be applied at the time of the débridement, the presence of infection not being considered a contraindication.

b. A thorough but careful early débridement is advisable.

c. Antigas and antitetanus serum should be administered prophylactically in all cases. Only too often is antigas serum omitted. The prophylactic use of these serums is again advised before delayed surgery is attempted.

d. Lacerations should be sutured early with interrupted silk sutures which may be easily removed if necessary.

e. The early intravenous use of blood serum or plasma is a great aid in the treatment of shock.

f. The use of the sulfonamides by mouth and locally is strongly recommended.

g. Sequestrectomy in chronic osteomyelitis should be thorough and include areas of osteosclerosis. In a slowly but steadily progressing molecular necrosis wide excision to areas obtaining their blood supply from collateral circulation, or amputation is indicated. Osteomyelitis of the lower third of the tibia, especially if involving the ankle joint, usually results in amputation and this is recommended early.

h. Syme's and Gritti-Stokes amputations are amputations of election. Amputation at the calf is usually to be condemned. A mid-thigh or Gritti-Stokes amputation is preferable.

i. Maggot therapy, although condemned by many, is an effective treatment for osteomyelitis, as is the Orr method.

j. Local irrigating solutions, antiseptics, and pastes of various kinds have not proved effective in the treatment of osteomyelitis.

PRECANCEROUS LESIONS

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BY definition, a precancerous lesion is one in which, statistically, the tissue is more likely to become invasive and metastasizing than is tissue involved in other, non-precancerous types of change. Since I have been asked to discuss precancerous lesions, and the exact phase of the topic was not specified, I infer that considerable latitude has been left to my judgment. I have chosen, accordingly, to discuss a view in which I am particularly interested and toward which all the investigative energies of my group have been directed for a number of years.

It would be redundant to present before this assembly the conventional statements regarding the changes which are considered to be precancerous. It is common knowledge that oral and vulval leucoplacia tend to become neoplastic, and that keratoses of the skin are very likely to do so. Less well known is the fact that only certain forms of mammary epithelial hyperplasia are prone to become malignant, and that the precancerous alterations of the gastric mucosa are not well understood. To obtain a better comprehension of the nature of the precancerous lesions, it is desirable to ascertain, from the study of those which have been proved, some common factor. Then, by the methods of modern scientific investigation, it should be possible to establish the means by which this common factor can be regularly induced in man and animals. Once such a mechanism were established, rational prophylaxis would follow logically; and only by the development of prophylactic methods are we likely to advance materially the cure of cancer, barring, of course, the occurrence of some major technical development.

What, then, is the common factor to be discerned in those changes which are known to tend to become neoplastic? In the skin, in the oral cavity, as well as in the hematopoietic apparatus, this common factor appears to be a chronic irritative one, but actually is probably an atrophy due to some mechanism which prevents the normal life and reproduction of the affected cells. Similarly, atrophy may well play a rôle, although as yet unproved, in the precancerous lesions of the genital organs, notably the breast, the uterus, and the prostate. At least one is safe in stating that cancer of these organs occurs at a time when their epithelium becomes functionally inactive, and when the metabolism of the specific chemicals, the sex hormones, which control their activity, becomes gravely altered. It is fair to assume, then, from the evidence, that the overgrowth which, when uncontrolled, is neoplastic, is in some instances a pathological response to the cause of the primary atrophic lesion. Obviously, then, it is desirable to establish clearly the cause of tissue atrophy in general.

In Table I are presented recognized examples of cancer which is known to follow the appearance of an atrophic process. Among these certain ones stand out as disorders without any known etiology. In at least three types, however, one can advance rather strongly suggestive evidence concerning causation. These types affect the skin, the liver, and the hematopoietic apparatus.

The evidence concerning the atrophic and precancerous lesions of the skin is clear, and needs little further discussion, since methods of measuring the function of its cells are not well established. As concerns the blood-forming organ, somewhat more information is available. From the observations of Hunter and Mallory, to which we have been able to add confirmatory evidence (3), it is clear that exposure to compounds of a known chemical structure, notably benzene, will cause, first, an atrophy and later the malignant overgrowth which we call leucemia. These changes are illustrated in Figs. 1 and 2.

Liver cancer, however, provides a particularly useful experimental tool, since in the animal it can be produced regularly under certain circumstances by a compound of known chemical constitution. Furthermore, in the animal sufficient

TABLE I.—PRECANCEROUS CHANGES

1. Skin
   - A. Keratoses of the atrophic skin
   - B. Xeroderma pigmentosa (atrophy)
   - C. Radiation dermatitis (atrophy)
   - D. Burn scars and lupus (atrophy)
   - E. Arsenic dermatitis (atrophy)
2. Kraurosis vulvae (atrophy)
3. Plummer-Vinson disease (atrophy)
4. Thyroid cancer after hypothyroidism
5. Cancer in undescended atrophic testicle
6. Cancer of liver on cirrhosis
7. Leucemia on aplastic anemia

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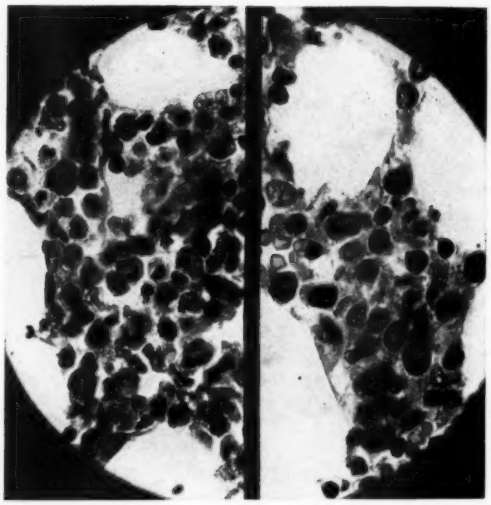

Fig. 1.

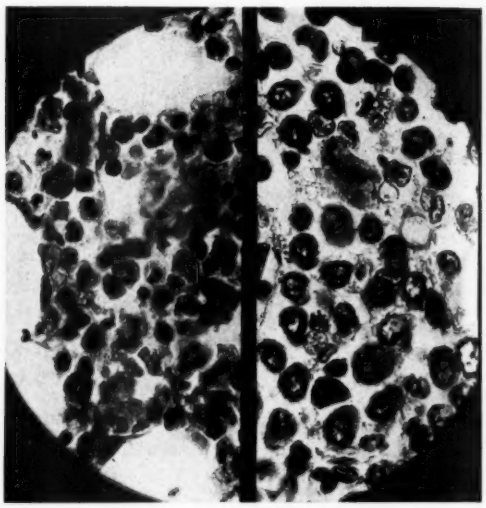

Fig. 2.

quantities of liver tissue for analysis can be made available easily. It is desirable, then, to examine the facts in order to ascertain to what extent liver cancer represents a primary atrophy followed by a malignant overgrowth, and how far experimental liver cancer is analogous to liver cancer in man. Kinosita has proved that the feeding of dimethylaminoazobenzene (butter yellow) to rats taking a diet of rice will produce regularly hepatic cirrhosis followed by hepatic cancer. Cirrhosis is clearly an atrophic process, and in this instance is precancerous.

How far can the analogy be drawn between this type of experimental neoplasms and liver cancer in man? Some points of similarity certainly exist. Human liver cancer tends to occur on a basis of cirrhosis, a point clearly proved by a recent communication from South Africa. In a very large series of patients with hepatic malignant neoplasms cirrhosis was always present.

What, then, is the nature of cirrhosis? Clearly it is a process which involves damage or death of normal liver cells and their replacement by regenerative tissue. How, then, can this basic process of atrophy be induced, and why should the regenerative effort of the liver give rise to cancer? The experiment of the Japanese workers previously described provided a method for the analysis of these problems. Obviously, it was desirable to ascertain how the combination of a rice diet and the administration of butter yellow operated to produce the primary cellular damage marked by atrophy. Kensler and Sugiura, in my laboratory, immediately attacked the problem. First they proved that the experiments described by the Japanese could be repeated regularly. Next the diets were analyzed to see what factor in them was lacking and was supplied by yeast. Third, the effect of butter yellow feeding on liver cells was examined; and fourth, the compounds into which butter yellow is broken down in the animal were isolated and identified. We proved that at least two factors were lacking in the diet which rendered the animals susceptible to liver cancer following the ingestion of butter yellow. The effect of the feeding of this carcinogen was found to be a poisoning of the activity in the liver cells of certain enzyme systems required for the respiration and metabolic function of normal cells. Here, then, was an explanation of the atrophic or precancerous process. Next the particular breakdown product of the chemical carcinogen which interfered with the respiration of normal cells was identified. Finally, certain evidence was obtained as to how this injurious effect was exerted. The fact became clear that the cancer-producing chemical induced atrophy of liver cells by competing successfully for the protein component of the cells without which their enzyme systems could not operate. If the efforts of the cancer-producing chemical to steal the enzyme protein could be directed into innocuous channels it would be possible to prevent the cancer-producing effect.

Why, then, does malignant overgrowth take place? All the details of this mechanism are, of course, not as yet worked out. One fact does appear clear, however. The cancer recurs and grows in the face of a milieu which is incompatible with the life and growth of normal cells. One would infer, therefore, that the cancer cell is malignant because it has developed some new way of life which renders it insusceptible to damage by the chemical compound employed in the experiment and concurrently immune to normal growth restraint. Were this the case, the compound involved in our experiments should stop the respiration of normal liver cells and not that of liver cancer cells. This is the case. Furthermore, this observation should be confirmable by another technique in another laboratory. Robert Chambers, at New York University, has confirmed the observation in tissue culture. Here, again, a concentration of a toxic breakdown product of butter yellow which will kill normal rat liver cells has no effect upon the growth and multiplication of liver cancer cells.

It may be argued that this type of fundamental work has no bearing on the problem of cancer in man. This may be the case, but if, as we assume from the results of the experiments described, the cancer cell is different in its respiratory mechanism from normal cells, it is not impossible that the future will provide us with effective chemotherapeutic agents.

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THE RÔLE OF THE RADIOLOGIST IN THE CANCER CLINIC

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DURING the past 25 years there has been a considerable advance in our knowledge of, and our interest in, the diagnosis and control of cancer. Early in this development it was recognized that some methods of attacking the problems should be devised which would bring together those physicians and scientists interested in the problem and which would permit the grouping of patients suffering from this disease for study and follow-up. In an attempt to solve this problem two plans have been developed which have received general acceptance throughout the world: namely, the cancer hospital, and the tumor clinic—both of these methods have advantages and disadvantages.

The cancer hospital is a considerably older development in point of time than the tumor clinic and, in general, it may be said that this method of approach has been more successful in fundamental research and in adding to our knowledge of the whole problem than has the tumor clinic. On the other hand, the tumor clinic has been outstanding in the therapeutic field and seems to be a better method of bringing a knowledge of the disease to physicians in general.

The cure of cancer is still largely a surgical problem. Irradiation being reserved for those patients who have passed the stage in which surgery can reasonably be expected to effect a cure or in whom for some reason surgery is contraindicated. If this general statement is accepted, the treatment of curable cancer then becomes largely a question of surgical skill. No one surgeon is equally skillful in operating upon all parts of the human body; surgeons have recognized this fact, and specialization takes place along anatomical lines rather than by disease. The surgeon working in a cancer hospital must of necessity confine himself almost wholly to the treatment of cancer, in some particular anatomical location, and it is questionable whether or not a surgeon would receive sufficient material for his proper development in a cancer hospital except in a few very large centers of population. As a matter of fact, most cancer hospitals do not attempt to treat cancer in all of its anatomical manifestations, as for example: tumors of the brain, lungs, and gastrointestinal tract. In most of the cancer hospitals today surgery plays a minor rôle, the major effort being devoted to research and radiation therapy.

The tumor clinic, on the other hand, offers an excellent opportunity for the development of surgical treatment in all fields of cancer. The operating surgeon in these clinics occupies an important position on the surgical staff of a large general hospital and the material which he has for study is ample. Another advantage of the tumor clinic is that its work is brought directly to the staff of the general hospital and to the practicing physicians of the community. In this way, these physicians obtain a first hand knowledge of the problem, rather than obtaining such information from occasional visits to large cancer centers or through the literature.

In so far as I am able to determine the first tumor clinic, as it is known today was established at the Massachusetts General Hospital in 1925 and grew out of a consultation service developed by the department of radiology dating back to 1919 when the first consultant was appointed to this clinic. At the Clinical Congress of the American College of Surgeons held in Philadelphia in 1930 Dr. Robert B. Greenough read a paper in which he described the work of the tumor clinic and told of its developments. The advantages of the clinic as stated by him at that time were as follows:

1. The work in cancer cases is placed in the hands of those members of the staff who are most interested in that subject.
2. Opportunity is given by consultation with representatives of the clinical, pathological, and radiotherapeutic departments for mutual instruction and increase of knowledge of the disease and its treatment.
3. A definite rational plan of treatment can be determined for each individual case, after consultation; and the results can be checked and discussed, by the group, in the subsequent follow-up.
4. Concentration of the hospital material permits greater experience and more productive work.
5. The standards of the hospital for efficient diagnosis and treatment of cancer are inevitably raised, and this educational effect extends beyond the hospital to medical students and to physicians in general practice in the immediate vicinity.

From the Massachusetts General Hospital.

Presented in the Cancer Symposium, before the Clinical Congress of the American College of Surgeons, Boston, November 3–7, 1941.

6. The additional expense to the hospital involved in the maintenance of the tumor clinic amounts only to about $3000.00 a year.

This report received the favorable attention of the College and the development of similar clinics in other centers has been largely due to their effort.

The personnel of a tumor clinic should consist of a surgeon, or better, a group of surgeons trained and interested in the treatment of cancer; a radiologist, or group of radiologists, similarly trained and interested in the problem; an internist; a pathologist; a social service worker; and one or more clerks and nurses. It is of the greatest importance that the physicians composing the staff be on a somewhat equal footing. The clinic should not be dominated by either the surgeon, the radiologist, the pathologist, or the clinician. The executive head of the clinic should be chosen for his personal qualifications and for his interests in the problem as a whole, rather than because of his position in any one field of medicine.

At the present time, at the Massachusetts General Hospital, the direction of the tumor clinic is in the hands of a committee which represents surgery, medicine, radiology, and pathology—the chairman of the committee being the chief surgeon. All appointments to the staff are approved by this committee on the recommendation of the chief of the service involved.

The tumor clinic acts primarily as a consulting and follow-up service. The treatment, whether it be surgical, medical, or radiological, is under the control of the chief of the general medical, surgical, or radiological service. Much of this treatment is handled by special assignment by members of the tumor clinic. In all cases recommendation by the tumor clinic regarding treatment receives serious consideration. It has been found advantageous to carry on a certain amount of minor surgery in the tumor clinic itself, such as the taking of specimens for biopsy or the removal of small superficial lesions. It has also been found desirable to hold the clinic in close contact with the x-ray therapeutic department; this encourages the follow-up of patients and makes available to the department of radiology immediate surgical or medical consultations. Patients referred to the clinic for consultation are first seen by the resident surgeon or radiologist assigned to the department and are referred to the specialty in which the location of their disease places them. Whether or not other specialists are asked to see the patient will depend largely upon the possibility of surgical, medical, or radiation therapy. The opinions given to the service referring the patients is that of the clinic as a whole, rather than of a single individual in most cases and in all controversial cases. Since the treatment of cancer in most cases at the present time is either surgical or radiological the selection of cases for these procedures is of great importance. In arriving at a decision many factors should be considered, most important of which are: the stage of the disease, histology of the tumor, the age and condition of the patient, the location of the tumor, and the chance of cure or relief by the various methods of treatment. It is not sufficient for the surgeon to state in a given case that he believes the disease is curable by surgery. He must also state the amount of permanent damage resulting from the operation and the risk; the same is true regarding the opinion of the radiologist. If, in the opinion of the surgeon, the tumor cannot be removed completely, or if the operative risk is too great, irradiation should be considered. An attempt to cure by irradiation usually results in considerable discomfort for the patient and in permanent damage to tissue in the radiated field. It should not be undertaken unless there is a reasonable chance of cure. Palliative treatment, on the other hand, will often control the disease for a considerable period of time and relieve suffering. It is important that this distinction be recognized and that the treatment be not too prolonged or severe with an incurable patient.

The selection of the kind of irradiation in a given case will depend largely upon the location and character of the tumor. The use of radium in our clinic has decreased rapidly during recent years and is now largely confined to treatment within accessible body cavities; an excellent example of which is the uterine cervix. It may be used to destroy a residual tumor after irradiation with x-ray, but this field of its use is definitely limited; needles or seeds should not be inserted where there is danger of infection. Since the use of radium at the present time requires, in most cases, a surgical operation we have found it more satisfactory to allow the surgeon to carry out the entire procedure rather than to call in a radiation therapist to apply the radium. The application of radium as used today is relatively simple and the surgeon can master the radiation technique with much greater ease than the radiologist can the surgical technique. The use of irradiation with x-ray, either preceding or following a surgical procedure, also has, in our opinion, a limited field of usage, although it has in the past been used extensively.

Postoperative irradiation, rarely if ever, cures a patient who was incurable by surgery in the beginning, although it may prolong the period in

which the patient is free of recurrence. Nor, will preoperative irradiation make an inoperable case operable. The feeling prevalent among some surgeons that, if the operation fails, irradiation may be used to effect a cure should be discouraged. An operation should not be attempted unless there is reasonable chance of cure. These patients are better handled by irradiation alone. Postoperative irradiation should be used in those cases in which, after operation, it is found necessary to change the original diagnosis; in those cases in which the surgeon realizes at the time of operation that he is unable to remove the tumor completely, or in which histological examination of the tumor following operation shows the disease to be of a high degree of malignancy. In this latter group, particularly if the tumor is known to be radiosensitive, preoperative irradiation in rather small doses may be found to be of value.

It has been our experience that the best results are obtained when the therapeutic procedure is planned after consultation between the surgeon and the radiologist. The procedure then is carried out as a joint undertaking in which either of the consultants may proceed independently calling the other in for consultation when his method has failed.

The tumor clinic affords an excellent opportunity for free discussion of the therapeutic procedure to be adopted in individual cases, and the end-results made available by the follow-up system allows a comparison of results.

Perhaps it may seem to you that I have wandered considerably from the subject which I was asked to discuss, namely: "The Rôle of the Radiologist in the Cancer Clinic," but to me it seemed necessary to state the fundamental principles involved in the management of a cancer clinic before attempting to answer the question—which, after all, can be stated in a few words.

The position of the radiologist in the tumor or cancer clinic is that of any other members of the professional staff: that of a consultant.

The physician in charge of the patient will make the final decision after he has received the advice of the various specialists connected with the clinic and the treatment accepted will be carried out by the physician or service to which the patient is referred; the physician should accept full responsibility once the patient is placed in his hands. In other words, if after consultation and discussion, surgical treatment is believed to be the method of choice, the responsibility should be in the hands of the surgeon in charge.

If, on the other hand, irradiation is considered the method of choice, the radiologist is responsible for its administration, and for the care of the patient during the time in which it is being administered.

Any attempt to direct the surgical procedure by the radiologist or the radiological procedure by the surgeon can result only in confusion.

Finally, the position of any specialist in the clinic depends to a large extent upon his ability, and his willingness to serve.

RADICAL SURGICAL TREATMENT FOR CARCINOMA OF THE CARDIAC END OF THE STOMACH

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IN a recent communication I called attention to the fact that the renewed interest in the surgical treatment of cancer of the thoracic esophagus has centered attention on a problem in abdominal surgery which has received little recognition in the past. I refer to carcinoma of the cardiac end of the stomach. In spite of rapid advances in the diagnostic methods of roentgenography, esophagoscopy and gastroscopy, and improvement in surgical technique, surprisingly few attempts have been made to extirpate cancer of the cardiac end of the stomach. The paucity of reports in surgical literature of this subject is noteworthy. Sustained interest in a subject such as the surgical treatment of cancer must be maintained by repeated and continued reports of encouraging progress in the fight against this disease. With this in mind, I would like to summarize my experience with the surgical treatment of carcinoma of the cardia to date, enlarging somewhat on a few of the details reported in the paper already referred to.

The cardia of the stomach may present considerable variation in size, shape, and position. In most individuals, the terminal one-half to three-quarters of an inch of esophagus lined by squamous epithelium, occupies an intra-abdominal position just below the diaphragm. It is known as the cardiac antrum. Operative experience has shown that the junction between esophagus and stomach is usually sharply defined and is indicated by an indentation on the greater curvature side, the incisura cardiaca. At the point of union with the esophagus, the musculature and mucous membrane of the stomach are thickened to form what I believe to be a cardiac sphincteric mechanism. Although the anatomy textbooks do not stress this point, I am convinced from clinical experience that the muscular thickening at the cardiac orifice acts as a sphincter to prevent regurgitation of gastric contents into the lower esophagus. The pars cardiaca is that portion of the stomach at, and just distal to, the point of union with the esophagus. It extends to the greater curvature side to include the upper part of the fundus. The cardiac orifice is usually situated at the level of the eleventh thoracic vertebra behind, and the seventh left chondrosternal junction in front. At the esophagocardiac junction, there is a sharp change in the histological characteristics of the mucous membrane. Above, the mucosa is of the squamous cell variety, while below, it assumes columnar characteristics. It is important to remember therefore that carcinomas originating in the cardia assume the histological features of an adenocarcinoma in contradistinction to the squamous cell tumors arising in the esophagus. An adenocarcinoma of the cardia may grow upward along the lower esophagus for a considerable distance. The biopsy specimen obtained by esophagoscopy will always indicate the origin of the tumor. It is important to stress this point because on numerous occasions I have heard the statement made that the finding of an adenocarcinoma in the lower esophagus often indicated malignant degeneration in misplaced gastric mucosa. This I believe to be completely inaccurate because a large operative experience has proved that every instance of adenocarcinoma of the esophagus has originated in the cardia or upper stomach.

It is important to stress what direction the lymph node spread may take from cancers of the upper end of the stomach. In general, the initial spread is toward the nodes in the gastrohepatic omentum and those located along the greater curvature near the incisura. Involvement of the peripancreatic nodes may occur late in the disease. In general, it may be said that adenocarcinomas arising at the cardia spread peripherally below the diaphragm toward the gastrohepatic or gastrocolic lymph nodes, depending in part, upon the location of the tumor with respect to the lesser or greater curvatures. Extension above the diaphragm to the nodes in the posterior mediastinum occurs not infrequently. Early metastatic involvement of the liver is a frequent finding. This is unpredictable and is dependent upon chance invasion of the gastric veins by tumor tissue with extension to the portal system. As with carcinoma elsewhere, the prognosis is materially altered when gross node involvement is demonstra-

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TABLE I.—ESSENTIAL DETAILS OF THE CASES REPORTED IN THIS PAPER

Patient Sex Age	Approximate duration of symptoms	Location of tumor cm.	Biopsy	Operation	Postoperative complications	Follow-up	Remarks
H. Z. M. 62	5 mos.	40	Adenocarcinoma	10–13–39 Abdominal exploration, inoperable.	None	Died of disease 4 months later	
L. S. M. 36	6 mos.	39	Adenocarcinoma	10–19–38 Thoracic exploration, inoperable, gastrostomy performed	Fulminating pneumonia at autopsy	Died on third day	At present time, would explore abdomen first to determine operability
M. M. M. 60	4 wks.	40	Adenocarcinoma	10–6–39 Transthoracic exploration, inoperable. Gastrostomy performed	None	Died 5 mos. later	At present time, would explore abdomen first to determine operability
S. R. F. 58	6 wks.	38	Adenocarcinoma	5–21–40 Abdominal exploration, transthoracic resection with anastomosis	None	Well 18 months postoperative	One lymph node showed involvement
A. M. M. 60	About 9 mos.	40	Adenocarcinoma	6–6–40 Abdominal exploration. Transthoracic resection with anastomosis	None	Well 17 months postoperative	No involved nodes found
C. L. M. 60	2 mos.	39	Adenocarcinoma	3–7–40 Abdominal exploration, inoperable. Spivack gastrostomy	None	Died of disease 3 mos. later	
H. S. M. 67	2 mos.	40	Adenocarcinoma	6–28–40 Abdominal exploration, inoperable	None	Died 4 mos. later of disease	
S. L. M. 48	10 wks.	35	Adenocarcinoma	12–28–40 Abdominal exploration, inoperable	None	Died 5 mos. later of disease	
G. K. F. 55	6 mos.	38	Adenocarcinoma	10–25–40 Abdominal exploration, inoperable. Janeway gastrostomy	None	Died 3½ mos. later of disease	
I. G. F. 52	8 wks.	39	Adenocarcinoma	6–28–40 Abdominal exploration, inoperable. Janeway gastrostomy	None	Died 6 mos. later of disease	
J. G. M. 46	6 mos.	40	Adenocarcinoma	3–10–41 Abdominal exploration. Transthoracic resection and anastomosis	None	Well 8 mos. postoperative	Associated lymph nodes removed with tumor showed involvement
H. C. M. 66	1 yr.	40	Adenocarcinoma	4–1–41 Abdominal exploration. Transthoracic resection and anastomosis	Coronary occlusion on 6th day. Autopsy	Died suddenly on 6th day	Length of history and operability noteworthy
I. L. M. 51	4 wks.	40	Adenocarcinoma	5–5–41 Abdominal exploration, inoperable	None	Still alive	
J. A. M. 49	3 mos.	39	Adenocarcinoma	1–26–39 Transthoracic resection and anastomosis	Cerebral embolus. Autopsy	Died on 3rd day	Lymph nodes showed involvement
M. B. F. 70	8 mos.	39	Adenocarcinoma	1–29–38 Abdominal exploration. Inoperable. Janeway gastrostomy	None	Died of disease 2 mos. later	
J. B. M. 62	4 mos.	40	Adenocarcinoma	10–5–39 Abdominal exploration, inoperable. Janeway gastrostomy	None	Died of disease 3 mos. later	
W. C. M. 47	3½ mos	39	Adenocarcinoma	10–25–39 Abdominal exploration, chest exploration, inoperable	None	Died of disease 4 mos. later	Extensive mediastinal node involvement
C. D. M. 56	5 mos.	36	Adenocarcinoma	2–1–38 Janeway gastrostomy. 4–19–38 Chest exploration, inoperable	Postoperative pneumonia	Died 1 mo. later	
L. E. F. 73	10 wks.	39	Adenocarcinoma	8–3–39 Transthoracic resection and anastomosis	Became comatose on 3rd day	Died on 4th day	Autopsy essentially negative
W. H. M. 49	6 wks.	40	Adenocarcinoma	6–20–39 Transthoracic resection and anastomosis 7–2–39 Right thoracotomy for pyopneumothorax	Developed ruptured lung abscess of right lung	Lived for 16 mos. Died of extensive retroperitoneal metastases	Resected specimen showed extensive node involvement

TABLE I.—ESSENTIAL DETAILS OF THE CASES REPORTED IN THIS PAPER—Continued

Patient Sex Age	Approximate duration of symptoms	Location of tumor cm.	Biopsy	Operation	Postoperative complications	Follow-up	Remarks
H. H. M. 39	6 wks.	40	Hodgkin's disease of cardia	4-12-41 Abdominal exploration, transthoracic resection and anastomosis	None	Doing well 7 months postoperative	This case is included in series for obvious reasons
M. F. M. 61	5 mos.	40	Negative biopsy	5-14-41 Exploratory laparotomy, inoperable	Several severe gastric hemorrhages	Still alive	
M. B. M. 57	3 mos.	40	Adenocarcinoma of cardia and lower esophagus	5-21-41 Exploratory laparotomy, transthoracic resection and esophagogastrostomy	Mediastinal abscess and peritonitis	Died on 9th day postoperative	Leakage from small perforation of esophagus at site of operative injury. Suture line intact
J. G. M. 57	3 mos.	40	Adenocarcinoma	6-4-41 Abdominal exploration, inoperable	None	Alive	
R. M. M. 55	4 wks.	39	Adenocarcinoma	8-6-41 Abdominal exploration, adherent to pancreas, metastases to diaphragm	None	Alive	

ble at operation. However, this should not deter the surgeon from carrying out radical extirpation of the growth and all the associated lymph nodes. Follow-up studies have demonstrated that a not inconsiderable proportion of such cases have survived the 5 year period. Metastatic involvement of the liver immediately classifies the case as inoperable. I do not believe that any patient with a resectable growth associated with hepatic involvement should be subjected to so extensive a procedure as a palliative measure.

The symptoms produced by a neoplasm at the cardia of the stomach will, in large part, depend upon the exact site of origin of the tumor and the direction of this growth. Cancers arising at the cardiac orifice quickly interfere with the act of deglutition and produce symptoms of lower substernal pain, especially on swallowing. These tumors usually extend upward to involve the lower esophagus. On the other hand, a tumor originating on the greater curvature side of the cardia, in the so-called silent area of the stomach, may produce no symptoms whatever until the growth has extended into the orifice itself. By the time dysphagia is noted by the patient, the carcinoma may very well have reached the inoperable stage. This type of case has been a factor in lending discouragement to active surgical treatment for cancers of the upper end of the stomach. However, it is important to emphasize that many of these patients may have persistent indigestion which resists medical treatment or that there may be an unexplained loss of weight. In such circumstances, it is imperative that the physician avail himself of every diagnostic method to demonstrate the presence of a tumor in this region. In general, the symptoms will depend upon the proximity of the tumor to the stream of swallowed food and the size of the growth with respect to diminution of the caliber of the cardiac orifice or lower esophagus.

In a number of instances, operative exploration has demonstrated extension of the growth beyond the wall of the stomach to the posterior parietes or to the body of the pancreas. These patients have complained of back pain usually located to the left of the midline at the level of the eleventh or twelfth thoracic vertebra. This symptom has generally occurred late in the disease. A careful evaluation of the symptom of persistent back pain is of considerable importance in estimating probable operability.

An analysis of the cases reported in this paper indicates that loss of weight does not reach the extremes frequently seen in operable squamous cell carcinomas of the esophagus and that when great weight loss has occurred, the tumor, in all probability, will be found to be inoperable by reason of extensive node involvement or extension to the liver. The question of weight loss, therefore, is of considerable importance to the surgeon in helping him to estimate operability.

Malignant degeneration of a pre-existing benign ulcer at the cardia brings up the ever recurring debatable problem. There were 3 instances in this series of a long-standing ulcer history with relief of symptoms by the usual medical therapy, and, in one instance, the x-ray films, fortunately preserved, taken 10 years ago, showed a small penetrating ulcer at the lesser curvature side of the cardia. In the latter case, symptoms became more persistent in the last few months and did not re-

spond to medical treatment. While the clinical and pathological evidence of malignant degeneration of a pre-existing ulcer in these cases is more speculative than real, the course of events is certainly most suggestive.

The general examination of a patient suspected of harboring a cancer of the cardia rarely yields positive findings. Occasionally one may demonstrate an enlarged lymph node in the left supraclavicular fossa, the Virchow node. Unusual hardness of this node or fixation to surrounding tissues is an indication for biopsy to demonstrate metastatic involvement. Rarely can one palpate the tumor on abdominal examination. Metastatic liver involvement may or may not be demonstrated by palpation. It is important not to omit rectal examination to exclude metastases to the rectal shelf.

Every patient presenting the symptoms enumerated should be referred to a competent radiologist for roentgenographic visualization of the esophagus and stomach. In most instances, the presence of a tumor will be clearly demonstrated by the usual methods. The most common roentgenographic findings are obstruction of the lower esophagus, irregular filling defects at the cardia, rigidity of the lesser curvature on fluoroscopic observation, and loss of the normal mucosal pattern. It may be extremely difficult to demonstrate any abnormality when the tumor is located on the posterior wall toward the incisura. Persistency on the part of the examiner with the aid of a heavier mixture of barium and the taking of multiple films in the lateral, oblique, reclining, and standing positions will usually demonstrate the growth.

Every patient presenting the symptom of dysphagia, associated with positive findings in the x-ray films, should, in my opinion, be subjected to esophagoscopic examination. This is an important part of the complete work-up. The esophagoscopist accurately locates the upper level of the tumor with respect to the distance of the upper incisor teeth and thereby guides the surgeon in his operative approach. Histological examination of the biopsy specimen will indicate whether the tumor has originated from the stomach mucosa, or from esophagus. I have preferred esophagoscopy to gastroscopy because, with the former, more accurate visualization of the tumor may be obtained, and at the same time, a biopsy specimen may be secured. In the hands of a competent operator there is little difference in the risk of the two procedures.

Once the decision to attempt radical extirpation of carcinoma of the cardia is made, a period of preparation for the ordeal is in order. In previous publications I have elaborated on the details of this pre-operative preparation and will not discuss them at this time. Suffice it to say that this should include careful attention to oral hygiene, a high caloric liquid diet, parenteral administration of vitamins, the administration of fluids by venoclysis, recently, the use of intravenous amino acids both before and after operation, and a preoperative transfusion of whole blood. On the basis of our favorable experience with the preoperative administration of sulfanilamide in colonic surgery, as reported by Garlock and Seley, I have routinely administered this drug to patients with cancer of the cardia for 72 hours prior to operation. It is my impression that this drug has been a considerable factor in minimizing infection. The recent report by Seley and Colp, concerning the bacteriological studies in cancer of the stomach, is confirmatory evidence of this opinion.

The demonstration of adenocarcinoma in the biopsy specimen will immediately indicate to the surgeon the plan of surgical attack to be adopted. There seems to be general agreement at the present time that the operation of choice for cancer of the lower esophagus and cardiac end of the stomach is a left transthoracic, transdiaphragmatic resection with intrathoracic esophagogastrostomy. Any other operative procedure which is limited to an abdominal approach falls far short of the ideal sought for in the radical surgical treatment of cancer anywhere, namely, free exposure and complete visualization of the field of operation. However, because the lymphatic spread of cancers of the cardia is most often in a peripheral direction *below the diaphragm*, it is important to determine operability without exposing the patient unnecessarily to the risks of a transthoracic exploration. For this reason, I suggested some time ago that exploration be carried out through a small upper left rectus incision. Palpation will quickly indicate whether the tumor is resectable. Metastases to the liver or to the pancreatic lymph nodes and fixation of the growth to neighboring vital structures are contraindications to further surgery. Rarely, abdominal exploration will indicate operability, yet, when the chest is opened, extensive mediastinal node involvement will be demonstrated. This, in my experience, is so infrequent that it may be considered only as a remote possibility.

If the tumor seems resectable, the wound may be closed quickly with buried figure of eight steel wire sutures and skin clips. The patient is now turned on his right side and, following a change in the operative setup, the left thoracic cavity is entered through the eighth interspace. Those

interested in the details of the operative procedure are referred to previous publications on the subject. Briefly, the operation, considerably modified from the original Fischer and Sauerbruch procedures, includes division of the eighth, seventh, and sixth ribs close to the spine, mobilization of the distal esophagus, radial incision of the left leaf of the diaphragm, mobilization of the upper two-thirds of the stomach by dividing the left gastric artery and the left gastroepiploic vessels, resection of the tumor-bearing portion with a wide margin of normal tissue, block dissection of the associated lymph nodes with the primary tumor, the performance of a two layer silk suture anastomosis between the end of the esophagus and the anterior wall of the stomach, and the telescoping of the esophagus into the stomach in order to obviate tension on the suture line. Under water drainage of the pleural cavity by a tube inserted through a stab wound in the subjacent intercostal space completes the operation. I believe it is important that every patient receive a transfusion during the course of the operation. In every case, I have employed positive pressure ethylene or cyclopropane anesthesia after a basal dose of avertin. Intratracheal anesthesia may also be used, provided that the trauma of intubation is minimal.

Reference should be made to the advisability of staging the operation so as to diminish the likelihood of operative shock. Marshall, in his case report in 1938, divided the operation into two stages. At the first operation, through an abdominal approach, the blood supply of the upper part of the stomach was ablated and the mobilized portion was pushed up into the posterior mediastinum through the surgically enlarged esophageal hiatus. Approximately 2 weeks later, the second stage was performed and consisted of a left transthoracic resection with anastomosis. My objection to staging the operation in this manner is threefold. In the first place, during the first stage, it is impossible to demonstrate mediastinal node involvement; second, it is technically easier to free the upper end of the stomach by the transthoracic, transdiaphragmatic approach than from the abdominal side, and in addition, the entire field of operation is more clearly visualized; and third, operative shock has not been a factor in the causes of postoperative mortality. If bleeding is carefully controlled, if tissue trauma is reduced to a minimum and if the patient is transfused during the course of the operation, surprisingly little shock will be noted. The operating time for the one stage procedure has varied between 2 hours and 2 hours and 30 minutes. For the reasons stated, I prefer the one stage operation.

Experience has proved that the operation of resection of the upper stomach with intrathoracic esophagogastrostomy is physiologically sound and that solid healing takes place at the site of suture. Including a group of squamous cell cancers of the distal esophagus, I have carried out this operation in 16 cases and in not one instance has there been any evidence of dehiscence of the suture line or leakage. I, therefore, see no reason for employing any of the complicated procedures to protect the suture line such as were recently reported and which were based only upon observations made in the experimental laboratory.

Before the operation is undertaken, it is important to explain to the patient that he must not swallow for a period of 4 or 5 days. The processes of repair at the suture line will be hastened by the full co-operation of the patient in this respect. Fluids are administered by a continuous intravenous drip of 5 per cent glucose in normal saline.

The character of the material draining through the intercostal tube will indicate the progress of the intrathoracic situation. During the first 48 hours, the fluid is sanguineous. After this, it gradually assumes a lighter color and decreases in amount until the seventh or eighth day when the tube may be removed.

Small sips of water may be given on the fourth or fifth day. Increasing amounts of liquid are given until the twelfth or thirteenth day when custards, gelatins, cereals, etc., are permitted. The diet is rapidly increased thereafter. Solid food should not be given until the third week.

As with adenocarcinoma of the rest of the gastrointestinal tract, the results of radiation therapy have been extremely disappointing. Even the direct exposure of the tumor by the use of a special intragastric tube, as reported by Pack and others has failed to show results sufficiently encouraging to warrant substituting this method of treatment for direct surgical attack. Unless obvious contraindications exist, I believe every patient with a cancer of the upper end of the stomach should be explored to determine operability. If this plan is followed, it is obvious that many more successful resections will be carried out.

RESULTS

During the past 4 years, I have explored 25 patients with adenocarcinoma of the cardiac end of the stomach. Nine were found operable, an operability percentage of 36. There was no operative mortality in the inoperable group. Nine patients were subjected to the radical operation. There were 4 postoperative deaths, an operative mortality of 44.4 per cent. Of the 5 survivors, 1 patient

died of retroperitoneal metastases 1½ years after operation. The 4 remaining patients are alive and well (no evidence of recurrence) 18 months, 17 months, 8 months, and 7 months, respectively. The essential details of the entire series are tabulated in Table I.

SUMMARY AND CONCLUSIONS

Until recently, cancer of the upper end of the stomach was generally considered beyond the scope of radical surgery and patients afflicted with the disease were placed in the hopeless group. With the development of the more accurate diagnostic procedures of roentgenography, esophagoscopy, and gastroscopy, an increasing number of patients in the early and perhaps curable stages of the disease is being referred for treatment. Whether such treatment should be by radiation methods or radical surgical extirpation, should, in my opinion, be a matter of little discussion. The results of radiation therapy of the most modern type have been universally disappointing and no cured case has, thus far, been recorded. On the other hand, with the modern improvements in surgical technique and recent advances in the field of anesthesia, surgery has much more to offer the patient harboring this disease. On the basis of the experience cited in this paper and in others already published, the patient with a resectable cancer of the upper end of the stomach has a 60 per cent chance of surviving the operation and an 80 per cent probability of living more than 2 years. It remains for the medical profession to be alive to the possibility of the existence of a cancer of the cardia in every patient who complains of persistent indigestion and difficulty in swallowing and to accept the operation of transthoracic resection with esophagogastrostomy as a standard procedure, one which offers the patient the best chance of being cured of his disease.

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TRENDS IN CANCER RESEARCH

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ON behalf of the National Cancer Institute, I wish to acknowledge our indebtedness to the American College of Surgeons, first, for improving the standards of tumor clinics, which has been of great value to us in the effective distribution of radium loans and in the provision of free training for physicians in diagnosis and treatment[1], and second, for having kept alive the constructive interest of the medical profession and laity in the cancer problem.

Trends in any field of research change with time as new facts are discovered. Up to the end of the last century cancer research was confined to descriptive observations on cancer in man. Isolated reports of cancer in other mammals were ignored. Speculation was rampant as to causation. A remarkable exception was the keen observation of Percival Pott who, in 1775, recognized the possible relationship of coal soot and cancer of the scrotum in chimney sweeps. A century later, Virchow's hypothesis focused attention on the tissue cells, which were supposed to undergo malignant transformation as a result of "chronic irritation." Subsequent modifications of the cell theory attributed cancer to embryonic cell rests or to abnormal conditions during regeneration of injured tissues. With the recognition of the parasitic origin of certain diseases, the search for a specific infectious agent for cancer was let loose and to some extent has continued to this day. In retrospect it is clear that each one of these attempts to explain the causation of cancer had the weakness of oversimplifying the problem. At last, at the end of the nineteenth century, Claude Bernard's plea for controlled experimentation was applied to the cancer problem. As a result a large number of new facts have been discovered. The following discussion is restricted to mammalian neoplasms.

The first important conclusion reached from experimental work is the high specificity of malignant cells. Each one of the many types breeds true *in vivo* and *in vitro*. For instance, a mammary carcinoma of the mouse transplanted into other susceptible mice reproduces itself in an unlimited series of generations. Furthermore, many types of malignant cells have been maintained in tissue culture for years without losing the ability to produce the specific tumors after being inoculated into the same strain of animals from which they were derived. The maintenance of such cultures over a long time requires an aseptic technique which is more strict than that used in surgery. The slightest infection as a rule causes the loss of cultures. It is difficult to bring these and other facts into harmony with the view that mammalian cancers are due to a specific infectious agent, especially since it has not been possible to isolate such agents from any tumors. Moreover, numerous attempts to produce curative serums without exception have failed. On the other hand it is established, both clinically and experimentally, that certain parasitic infections can predispose tissues to the development of cancer, but it should again be emphasized that these parasites do not play a specific rôle and are not detectable in the resulting neoplasms.

Basing their investigation on Pott's observation, Yamagiwa and Ichikawa in 1915 announced the production of skin cancer in rabbits by the long continued topical application of coal tar. This important discovery shifted the trend of cancer research into the field of chemistry. Through painstaking work a highly potent carcinogenic chemical, 3, 4-benzpyrene, was isolated from coal tar. At present the carcinogenic properties of about 250 synthetic chemicals have been recognized. Some of these, as 20-methylcholanthrene, have been extremely valuable for the experimental production in animals of almost every type of malignant tumor seen in man. Fractions of a milligram of this compound can produce malignant tumors at the site of injection or in distant organs.

The ease of chemical carcinogenesis has thrown much light on tumor histogenesis under controlled conditions (3, 6, 7). Morphologically recognizable tissue injury may occur but does not necessarily precede tumor formation. As exceptions, I mention induced as well as spontaneous pulmonary and mammary tumors. In fact, the term "chronic irritation," while still of value for cancer-control education, has outlived much of its scientific use-

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[1]These activities are authorized under the National Cancer Institute Act.

fulness in cancer research. The conversion of normal into malignant cells is apparently due to changes which are far too subtle to be analyzed exhaustively by the available histologic methods. Even the most refined cytologic technique at present fails to differentiate malignant cells from the cells of origin. After all, what we see through the microscope is only an infinitesimal part of what is present and going on in living cells. For this reason I have maintained for some years that carcinogenesis, as well as other fundamental cancer problems, should be attacked from the viewpoint of cell physiology and biochemistry, for we are dealing with a fundamental biological problem.

Work with chemical carcinogens has firmly established the fact that tumors appear only after a relatively long latent period, which depends on the type, dose, and method of administration of the chemical, the animal species and strain, and the sex (2). The great value of animals with a relatively short life span of 2 to 3 years, such as mice and rats, may well be due in part to the rapidity of aging, which may be assumed also to speed up the cancer process. The physiological time factor is certainly important in human and animal carcinogenesis. Therefore, a better understanding of carcinogenesis will go hand in hand with a better understanding of the process of aging of which we know relatively little.

Another remarkable fact is the ease with which such a powerful chemical as methylcholanthrene can produce malignancies in a great variety of tissues, as the brain, skin, striated muscle, subcutaneous tissue, lung, et cetera. This lack of specificity with regard to the cell type involved deserves further study. It is, indeed, exceedingly important to explain the intricate mechanism of action of methylcholanthrene on any normal cell type which is known to be convertible into the malignant state. Work on this subject has been in progress for some time at the National Cancer Institute and elsewhere. We have found, for instance, that prolonged exposure of cultures of normal subcutaneous mouse fibroblasts to high dilutions of methylcholanthrene causes apparently permanent changes in cell physiology, comparable with those observed in cultures of sarcomas induced by methylcholanthrene in the subcutaneous tissue of mice of the same strain (4). Efforts are being continued to prove that carcinogenesis can take place *in vitro*. Positive results would be of great theoretical interest, since this would indicate that carcinogenesis does *not* depend on favorable systemic conditions, but can be explained by a direct interaction between carcinogen and cell.

Recently some progress has been made in the study of the dietary factor in the production of induced tumors. Tissue cells are highly organized biochemical units. Their normal function depends partly on a continuous supply of energy-yielding chemicals and of other chemicals which are needed for the construction of cell proteins, lipids, and carbohydrates, or for the regulation of cell activity, as enzymes and vitamins. Hence it is logical to consider the composition of the diet as a possible modifying factor in carcinogenesis. Some years ago, we (19, 20) showed that the growth rate of spontaneous mammary carcinomas in mice could be strikingly inhibited by diets deficient in certain essential amino acids. This inhibition of tumor growth was not accompanied by any evidence of general malnutrition. Recently other workers found that the development of hepatomas in rats induced by the azo dye, butter yellow, can be considerably delayed by certain diets (16). Work at our Institute (23) has also shown that the response of mice to skin painting with methylcholanthrene is strikingly influenced by the composition of the diet. If the diet contains an adequate amount of the amino acid, cystine, the mice develop acute leucemia with great regularity. On a low cystine diet, however, the development of leucemia is greatly retarded, and instead the mice exhibit extensive sclerotic lesions of the larger arteries.

Butter yellow and methylcholanthrene are toxic for young rats maintained on a diet low in cystine. The growth rate is strikingly inhibited and is accelerated as soon as cystine is added to the diet (22, 24). Dietary cystine may be regarded as a detoxicating agent for the two chemical carcinogens in question. Hepatoma formation by butter yellow is accompanied by severe liver injury and liver cirrhosis, which may or may not be a requisite for hepatoma formation (5). It is not easy, therefore, to differentiate the specific carcinogenic action from the nonspecific toxicity. Similar work on spontaneous tumors has also yielded results indicating a dietary influence.[1]

It has been suggested that abnormal diets may play a part in the causation of gastrointestinal tumors, an idea which at least has the merit of stimulating research. Roffo reported that rats which are maintained for a long time on a diet containing boiled fats develop gastric adenocarcinoma. Careful work at our Institute so far has

[1]Drs. White and Andervont, of this Institute, recently made the following observations. Virgin C3H mice when 4 weeks of age were divided into 2 groups. One group was fed a relatively low protein-low cystine diet and the other a relatively low protein-high cystine diet. At the end of 10 months all mice on the high cystine diet had developed spontaneous mammary tumors, whereas at 15 months none of the mice on the low cystine diet had mammary tumors.

not confirmed this claim. On the other hand, we have succeeded in producing for the first time gastrointestinal carcinoma in mice by means of methylcholanthrene (15). The forestomach of the mouse is lined by squamous epithelium and the rest of the organ by glandular mucosa. Spontaneous gastrointestinal tumors have never been observed in the mice used. At first the carcinogen was given continuously to the mice as a dilute emulsion in the drinking water. After many months there occurred squamous cell carcinomas in the forestomach, whereas the glandular portion was normal. Some of the animals also developed typical carcinoma of the small intestine (13). This curious susceptibility to malignant change of gastric squamous epithelium and the apparent lack of susceptibility of the gastric glandular mucosa must be explained. Can it be due to the inability of the carcinogen to penetrate into the gastric mucosa? To test this, a small volume of a dispersion of methylcholanthrene was injected into the glandular mucosa of mice of the same strains. Up to the present five typical adenocarcinomas have thus been produced at the site of injection. One of these tumors has been successfully transplanted subcutaneously into other mice. The transplants grow rapidly, and the tumors have retained their histological structure in two generations. To me the most interesting point is the probability that the layer of gastric mucus functions as a protective barrier when the carcinogen is given orally. If this be true, it follows that the production of gastric adenocarcinoma by carcinogenic dietary components, if such exist, may be conditioned by a break in the mucus barrier under pathological conditions.

The discovery of the artificial chemical carcinogens is a milestone in cancer research as it has made possible the experimental production of tumors under controlled conditions. Nevertheless, the great unsolved problem still is the causation of so called spontaneous neoplasms. The ease with which the artificial agents produce tumors strengthens the belief that the naturally occurring tumors are caused by chemicals formed within the body. In fact, it is firmly established that very large doses of female sex hormones acting over a long time can induce malignant tumors of the breast and uterus in mice and rats. Furthermore, experiments with different inbred strains of mice have revealed a unique influence of the mother's milk on the development of mammary cancer in the offspring (1). Foster nursing of newly born female mice from a strain with a normally high tumor incidence by a mother of a low tumor strain strikingly decreases the tumor incidence in the foster nursed animals. On the other hand, foster nursing of young females from a strain with a normally low tumor incidence by a mother of a high tumor strain greatly increases the tumor incidence in the fostered mice. Work on the nature of the agents responsible for these effects is in progress at our Institute, as is also the question as to whether or not the findings apply to human mammary carcinoma.

Mention may now be made of recent claims of the carcinogenic action of cell free extracts of tissues and of urine from cancer patients. This work is based on the assumption that as a consequence of abnormal metabolism endogenic substances exert a carcinogenic action. The first report in this field was made by the Russian scientist Shabad (12). He extracted grossly normal livers of individuals dead from cancer of the stomach, lung, and other organs, with benzene, since benzene is a good solvent for many carcinogenic hydrocarbons, sterols, and bile acids. After evaporation of the benzene extract the residue was injected subcutaneously into mice. This caused local tissue destruction and killed some of the animals. Malignant tumors were observed after 8 months or longer, both at the injection site and in distant organs. Few tumors also occurred in nontreated control mice. Similar results have been reported by British and American investigators. Taken as a whole, these findings should be accepted with considerable caution. While there is no doubt that malignant tumors were observed, it is premature to accept this evidence as conclusive proof for the existence of endogenic carcinogenic chemicals in cancer patients. Most of the tumors appeared after a very long latent period and in a relatively low percentage of injected animals. Sesame oil was used by some as a solvent, an oil which is known to cause subcutaneous sarcomas occasionally. Other workers used a rather drastic chemical method for the preparation of the test material, which leaves some doubt as to whether the carcinogenic material was preformed. Final proof must wait, therefore, until the agents are isolated in chemically pure form and until it is shown that the alleged active compounds occur in the body in sufficient concentration and can act over a sufficient time to induce tumors. This line of investigation serves as an illustration of the great effort and time required to establish fundamental facts in cancer research.

Brief mention should now be made of work designed to explain the difference in behavior of malignant and normal cells. Here again the biochemical approach seems to be advantageous

since it is reasonable to suppose that the difference in behavior may be due to differences in biochemical organization. One of the chief difficulties is the availability of a suitable control tissue for a given tumor (17). We have recently used with some success the normal and regenerating liver of the rat for comparison with a rat hepatoma. The regenerating liver serves as a comparison of a proliferating normal tissue with the proliferating liver tumor. The results so far obtained indicate that the tumor is characterized by a high anaerobic and aerobic lactic acid production and a respiratory quotient below unity[1], by a very low content in riboflavin (10) and coenzyme (11), by a great reduction in glycogen (6) with an apparent unchanged amylase activity, and, most striking, by a reduction in the catalase activity to one one-thousandth of that of the normal control tissues (9). The activity of some other enzymes seems to be unchanged. In short, it appears that some of the important enzymatic activities of the tumor show marked decreases, which may perhaps account for the specific tumor biology. It is evident that whatever differences have been found are of a quantitative, not a qualitative nature.

Another line of inquiry which in the past has been ignored deals with the systemic influence of cancerous growth as evidenced by cancer cachexia. Here again biochemistry may be helpful[2]. I have just referred to the great diminution of catalase in the rat hepatoma. Work at the Institute has shown that the catalase activity of the morphologically normal liver of rats carrying a large subcutaneous hepatoma transplant is reduced to less than one-tenth of that of the liver catalase of a normal rat. This effect is easily reversible, because after extirpation of the tumor the liver catalase returns to normal within 48 hours (8). Since catalase functions in the chain of oxidative reactions in tissue metabolism, it is rather interesting to find a very great reduction in catalase activity in the hepatic tumor and a lesser decrease in the apparently normal liver of the tumor-bearing animal. Unpublished data indicate that this decrease in liver catalase occurs also with other rapidly growing malignant tumors. Further studies may lead to information of use for correcting the pathological cancer metabolism.

As to research on diagnosis and treatment, I must refer to my Barnard lecture of a year ago (18).

[1]Work carried out in the Department of Biochemistry, Cornell Medical School.

[2]The first indication of a systemic biochemical action of the growth of two malignant tumors was reported some years ago (21). It was found that the nonprotein sulfhydryl compounds in certain tissues of the tumor-bearing animals showed a progressive decrease with increasing tumor growth.

CONCLUSION

In conclusion, I have tried to formulate some phases of cancer research and to report in a general way on the progress which is being made. Emphasis has been placed on the study of carcinogenesis, since hope of preventing cancer, not only the so called occupational but also the spontaneous neoplasms, must be based on such studies. I have also stressed the importance of work aiming at a better understanding of the behavior of cancer cells in comparison with the normal cells of origin. Great difficulties are met in the study of these problems in human beings. The limitations of purely morphologic studies were mentioned and the value of a physiologic and biochemical approach was pointed out. The outlook is good for further progress from combined laboratory and clinical research. Under present world conditions, the main responsibility for such studies for years will rest on American investigators.

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THE IMPORTANCE OF A COMPLETE DIAGNOSIS TO A SUCCESSFUL TREATMENT OF STRABISMUS

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As in all branches of medicine, a complete diagnosis must be made before an intelligent course of treatment can be instituted with any hope of a successful termination. The day is past when convergent strabismus can be considered always due to hypermetropia and a divergent strabismus due to myopia or to a so called anomalous position of rest.

A divergent strabismus is not uncommon in a high hyperope, nor is a convergent strabismus uncommon in a myope of even a low degree.

A vertical strabismus may be seen occasionally without an elevator or depressor being involved—in other words, due to an anomaly of sursumvergence—but in my experience this is most unusual.

The usual observation is that a large percentage of cases of lateral strabismus have a vertical element, which is a varying factor in the development of the lateral squint.

A certain number of cases of convergent strabismus of the convergence excess type are corrected completely by a full correction of the hypermetropia, augmented if necessary by orthoptic training, but many cases of low or high degree of hypermetropia are but little, if any, affected by a correction of the ametropia. Many patients are seen with a hypermetropia of low degree and a strabismus of 60 to 80 prism diopters; or again, with a hypermetropia from 2 diopters up, in which a full correction of the ametropia has really no appreciable effect on the strabismus. Discussion of the various theories has continued many years but our patients come and go while we are trying to find one solution to the whole problem as to diagnosis and treatment, be it operative or nonoperative.

I must quote again from McReynolds, of Dallas, who said in my hearing, "Every ophthalmologist who has ever had insomnia has devised a new operation or modification of a former procedure for the surgical correction of convergent strabismus, and, furthermore, every ophthalmologist has at some time had insomnia."

I believe that the unsatisfactory results from operations and the unsuccessful search for one procedure that will be generally adopted for the correction of squints are due to the failure of the operator properly to determine and evaluate the several factors that may enter into the production of any given squint, and that nonsurgical or surgical treatment will vary as the exact type of strabismus varies. This statement includes convergent, divergent, and vertical squints and any combination of these.

Stated briefly, the various factors entering into the production of squints are:

1. An anomaly of one or more of the individual muscles. This may be from a faulty structure of the muscles, from a faulty insertion of the muscles or from a faulty innervation. Each of these may have an added anomaly due to secondary contracture, secondary deviation, or to a primarily overacting muscle, as is occasionally seen in the large hypertrophic muscles.

Hence any squint should be studied first as to the possibility of an anomaly of any of the extraocular muscles.

2. The disjunctive acts of convergence, divergence, and sursumvergence.

Given a case of convergent strabismus in which individual muscle involvement has been eliminated, is the deviation greater for distance than for near? If greater for distance, it proves quite conclusively a primary divergence insufficiency, but if it is greater for near, it is primarily a convergence excess. If it is determined to be a convergence excess, is it due to hypermetropia, myopia, to a vertical imbalance, or may it be due to some systemic cause, as chorea, or even a lesser nervous irritation?

If a divergent strabismus is present and again the individual lateral muscles are normal, is the deviation greater for distance than for near? If greater for distance, it is a primary divergence excess, but if greater for near, it is primarily a convergence insufficiency. In either case, is the condition caused or modified by the kind or amount of ametropia or may an associated vertical imbalance be a main or contributing factor? In a conversation with F. W. Marlow, I stated that I believed that over 70 per cent of cases of divergence excess had a vertical anomaly. He had statistics to prove that nearer 85 per cent were so complicated. My experience is that most cases of

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anomalies of sursumvergence are primarily due to a vertical anomaly of another variety.

TESTS

Examination should include tests to determine deviation for distance and for near. At some time in the examination, these tests should be made with and without any ametropia being corrected. The effect of complete cycloplegia should be noted, also the correction of any vertical anomaly. The deviation should be measured in the 6 cardinal fields and, if a strabismus, the fixing eye in each field should be determined. The power of convergence should be studied and it should be determined whether this is affected by correction of an ametropia or vertical imbalance. The presence and degree of binocular fixation or suppression should be determined. The history of heredity, illness, birth, or other injuries should be investigated. Not the least of the contributing factors is the nervous mechanism of the patient.

Squints may be caused by chorea, hysteria, and other neurological conditions. If it is possible for these to be the sole cause, how probable it is that they may be a contributing factor, when hypermetropia, myopia, astigmatism, or any of the afore mentioned causes are present. Very frequently the convergent strabismus is worse when the patient is ill, overtired, or excited; or a divergent strabismus is noticed only when a child is "day dreaming."

When one has clearly in mind the things to be observed, the method of testing may be quite optional. It is unnecessary to state that my preference is for the cover test with the amounts of deviation measured by prisms. It is purely an objective test, can be used in any patient who has vision enough or is old enough to fix any chosen object, and it depends solely on the examiner's understanding of muscle anomalies and upon his powers of observation.

TREATMENT

After consideration of a patient with these different factors in mind and with some estimation of their relative importance in producing the given squint, treatment can be intelligently begun.

If, for example, glasses definitely lessen the strabismus almost at once, one is encouraged to expect a continued improvement, but if they have little or no effect within a month, then another factor is present which has not been given its due importance. This may be any one or more of the causes stated previously. Orthoptic training is in some cases a most helpful adjunct, but when orthoptic training is prescribed to a majority of patients with heterotropia, it is done through ignorance or dishonesty and may do much harm. Orthoptic training has a larger field in heterophoria, but even here the field of usefulness is definitely limited.

As soon as the ophthalmologist has determined that the results from different forms of nonoperative treatment are not giving the desired results or knows from experience that any form of nonoperative treatment will be a disappointment and expense, then surgery should be considered and the sooner the better.

SUMMARY

1. An examination should be made as soon as a muscle anomaly is observed or suspected.

2. If it is impossible to make an exact differential diagnosis at once, the patient should be re-examined at intervals until such diagnosis is made.

3. The effect of various methods of treatment should be observed, by using those that will most probably prove the points in question.

4. These methods include consideration of the effects of cycloplegics, correction of an existing ametropia, correction of a vertical imbalance, and the results of the fusional tests and orthoptic training.

5. A complex either of inferiority or of defense commonly develops in cases of strabismus and often at a very early age.

6. When a patient so studied fails to respond satisfactorily to any probable nonoperative treatment, surgery should be considered and before school age unless there is a definite contraindication.

SURGICAL MANAGEMENT OF HETEROPHORIA

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HETEROPHORIA may be defined as a break in the amplitude of fusion, or the decompensation of muscle balance is maintained by fusion and the neuromuscular mechanism. Having diagnosed the presence and type of a phoria, the question of treatment presents itself. The diagnosis and the medical treatment with glasses, prisms, and orthoptic exercises, is not the function of this assignment. These most important points have been or will be discussed in the symposium. But it is necessary to emphasize that the decision to operate rests squarely on them. The analysis of the individual case is the prime requisite of surgical judgment. Success or failure in ocular muscle surgery particularly, depends entirely on the accuracy of our presurgical study and conclusions.

Lancaster said "the two things for which we strive in operating are, first, a position of orthophoria since, other things being equal, the nearer the eyes to a position of orthophoria, the less the task of the neuromuscular mechanism in maintaining binocular vision; second, an effective range of fusion, this being, if possible, even more important than the former. A neuromuscular mechanism, for example, may be made to produce an orthophoria by so shifting the position of the eyes in the orbits that approximately the same working of the controls will now result in orthophoria because the eyes start from a position nearer the ideal one. The idea that the purpose of operating on the ocular muscle is to weaken or to strengthen some muscle which is too strong or too weak is unsound physiologically."

Having concluded that operation is necessary, a conclusion often arrived at only after repeated interval observations, two questions arise: (1) when to operate, (2) what to do and how much.

The first question can be simply answered. I think that one should operate when a phoria produces symptoms that can be relieved in no other way, provided that there is some degree of fusion power available and capable of being increased in its amplitude. This is particularly applicable to hyperphoria when it may happen that the patient has not suppression of the false image but it does not cause trouble because it is so far from the true image. The more closely the false image is approached to the true one without fusion the more annoying it becomes. Such patients are not grateful.

The age of the patient, I believe, makes little difference although it seems wise to overcorrect an exophoria and undercorrect an esophoria in the very young (under 8 years). It has been my experience that adduction decreases and abduction increases with age. Phorias, particularly of high degree, may easily develop into tropias without the child complaining. It is easier to learn suppression when very young and when the fusion impulse is not as strong as it is later. Older children and particularly adults, complain of diplopia, occasionally for a long time, when fusion decompensation occurs. Such decompensation may occur as the result of age, illness, or fatigue. The learning of suppression takes much longer in these cases and for that reason the adult himself seeks relief from the annoying diplopia.

The second problem, what to do surgically, and how much, is more difficult of solution. I shall leave to our distinguished South American confrère, Dr. Alvaro, the task of describing the modern surgical techniques employed in squint, since these maneuvers are the same for the phorias as for the tropias, with few exceptions. The choice of the type of operation is that with which the surgeon is thoroughly experienced and skilled.

Since the object of surgery in the phorias is to facilitate fusion, it is not necessary to do as much, I think, as in the tropias. In other words, it seems better to do too little than too much. Although with modern materials and techniques the chances of sutures slipping and making matters worse are not nearly as great as hitherto, such cases do occur and must be guarded against. For this reason it would seem better to restrict the operations to recession or at least controlled or partial tenotomy for lengthening, and tucking or the O'Connor cinch operations for shortening.

The choice of an anesthetic is that of individual opinion. Many prefer local anesthesia, injecting the anesthetic well back into the belly of the muscle in the orbit in order to obviate, if possible, the annoying edema of the muscle at its attachment. A general anesthetic, particularly when given through an intratracheal tube thereby freeing the field of cumbersome masks, appears to be

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ideal for all ages, provided, of course, that there are no contraindications.

Whatever operation is done must be done meticulously. The various steps of the operation from the conjunctival incision to its final closure must be methodical, painstaking, and surgically precise. Tenon's capsule must be preserved as far as possible, the muscle and tendon bruised as little as is necessary and the wound closed completely if one wishes to avoid postoperative trouble.

Since we are dealing with living tissue and not mathematic figures the problem of just how much to do is indeed a thorny one. Many times it appears to be solved only by intuition based on many years of bitter experience. The causes of failure are many and discouraging, but if a proper analysis of the case has been made, particularly the investigation of hyperphoria, the percentage of failures will necessarily decrease. Too often is the presence of hyperphoria missed. It is much more common than thought, as can be seen by the analysis of 1,955 cases of ocular motor anomalies by White and Brown, who found that 36.6 per cent had an accompanying vertical anomaly. They concluded:

"In uncomplicated convergence excess with either a lower or a higher degree of hypermetropia, a double recession will give a most satisfactory result. However, when a vertical imbalance is present, the same amount of recession for an equal amount of lateral squint may result occasionally in undercorrection but more frequently in overcorrection, about as much as the original squint. This result may be delayed or it may develop immediately after operation.

"In uncomplicated divergence excess with a normal convergence near-point, a conservative recession of one or both external rectus muscles gives a good result. In the presence of a vertical imbalance, there may be an undercorrection, but much more probably a marked overcorrection.

"In convergence insufficiency with secondary divergence excess, or when the divergence excess is primary, one can judge the operative results accurately when there is no vertical imbalance. But in the presence of a complicating hypertropia, the same amount of recession or resection may result in a definite overcorrection, but much more probably there will be an undercorrection of the lateral deviation.

"These failures will become less frequent if the vertical imbalance can be corrected before the lateral imbalance."

Certain general rules have been laid down by the experience of others in an effort to determine what to do in average cases. A table of such rules can be found in Spaeth's *Principles and Practice of Ophthalmic Surgery*; because it will be found useful as a starting point it is worthy of emphasis.

The rules for hyperphoria must be briefly and vaguely stated. It is agreed that surgery should be directed to the hypophoric eye, although it may be necessary to divide this between the two because of a great degree of hyperphoria. It should be recalled that double hyperphoria is usually not a surgical condition but is a pure innervational defect. Operation, however, should be considered at times when the double hyperphoria is decidedly unequal. One should do either a recession of the overacting muscle or tucking or the cinch operation on the underacting muscle in the hypophoric eye, combined with operation on the hyperphoric eye as may be indicated. It is, indeed, wise to do a little at a time in the correction of a hyperphoria, rather than too much at one sitting. Sometimes one should allow an interval of time, for example, 2 to 3 months, between operations on the vertical muscles. During this interval orthoptic exercises may be used with advantage. The surgical correction of hyperphoria is fraught with difficulties and errors of judgment and constitutes the most difficult problem in ophthalmic surgery.

TABLE I.—RULES FOR DECIDING ON SURGICAL PROCEDURES FOR THE PHORIAS (SPAETH)

I Phoria	Individual type	Surgery
Exophoria	Accommodative exophoria as with myopia, convergence insufficiency near only, proportionate to degree of myopia	Tucking or cinch of one or both internal recti
	Convergence insufficiency exophoria for near and distance, measurement of prism ductions show duction defect to be in the disturbed adduction-abduction ratio	Tucking or cinch of one or both internal recti. May need recession of one external rectus as well
	Divergence excess, exophoria for both near and distance. Abduction>adduction	Recession of both external recti
Esophoria	Convergence excess. Adduction greater than abduction	Recession of both internal recti
	Divergence insufficiency	Tucking or cinch of one or both external recti

The same can be said for cyclophoria. Indeed, so easily can this condition be made worse, from the patient's viewpoint, that only the most expert muscle surgeon should tackle this problem.

One can conclude, therefore, by reiterating the statement that the surgical management of heterophoria depends fundamentally on the accurate diagnosis and skillful analysis of its factors, and that each case is a law unto itself. The diagnosis and not the actual performance is what counts.

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TUMORS OF THE SALIVARY GLANDS, BENIGN AND LOCALLY MALIGNANT

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SALIVARY gland tumors are probably the most debatable of all tumors and have been for many years. There are those which are definitely benign and those which are definitely malignant, but the largest group and most controversial is the mixed tumor which is benign in that it rarely metastasizes but malignant in that local recurrence is a predominating characteristic.

Parotid cysts may be congenital, but they are usually secondary to chronic infection or duct obstruction. They are often without symptoms but more often marked by the presence of swelling over the gland with pain and tenderness which may disappear with the emptying of the accumulated salivary secretion by opening of the ducts. After a time the obstruction becomes more complete with infection complicating the picture. When suppuration occurs, external drainage may be resorted to. Following drainage complicating salivary fistulas may result; therefore, every effort should be made to avoid operative interference. In several instances, we have seen these troublesome cystic glands cured by x-ray therapy. If sufficient radiation is given, the gland atrophies, becoming functionless, and the cysts give no further trouble. This is a great improvement over former attempts to dissect out the cysts.

Mikulicz's disease, because of the peculiarity of the condition and the unexplained etiology, cannot be ignored in the discussion of tumors of the salivary glands. While enlargement of the salivary, particularly the parotid, and lacrimal glands may be associated with leucemia, tuberculosis, lymphosarcoma, and toxic conditions, and has been given the name of Mikulicz's syndrome, the condition described by Mikulicz in 1888 was a definite condition without constitutional symptoms. The important part of the pathological anatomy of the disease is an extensive deposit of small round cells which seem to compress or displace the glandular parenchyma. These cells appear to be either an infiltration of leucocytes or multiplying lymphoid tissue ordinarily found in the gland. The gland structure may be compressed or infiltrated with an excess of fibrous tissue as well. While the prognosis in these cases is difficult because of their rarity and the absence of final reports upon cases found in the literature, we think we can safely say that they are not serious and treatment is unnecessary. A case we observed exhibited no symptoms and little change in the condition over a 5 year period although the tumefaction was marked. Cases are reported in which the lacrimal glands have had to be removed because of pressure upon the eyeball. Radiation should, and apparently does, have a beneficial effect in preventing the progress of the disease.

Adenolymphoma (onkocytoma) of the parotid gland is one of the rarest of tumors. It may not be directly in the salivary glands but often adjacent to them. It is composed of a lymphadenoid stroma with germinal centers with an epithelial structure in the form of tubular glands, cysts, and papillae (papillary cystadenolymphoma or papillary cystadenoma lymphomatosum). They occur in older people, are benign, encapsulated, and grow slowly. They are not usually intimately connected with the gland and may be easily removed without damage to the facial nerve or danger of recurrence.

Adenoma of the salivary gland is again one of the controversial tumors, and Warren (8) says, "Adenomas readily recognized as such are extremely rare in the salivary gland." If they do occur, it is in the parotid gland. They are always encapsulated and may be cystic or solid. The differential diagnosis between the adenoma and mixed tumor is hardly possible before operation.

Mixed tumors comprise the great majority of all tumors of the salivary glands and have been of particular interest to the profession for many years. The literature is fairly rich in discussions of this particular neoplasm. Because of the large size they may attain, years ago surgical attempts were made to remove them. I. S. Cutter wrote an interesting account of a controversy between the medical departments of the University of Pennsylvania and Jefferson Medical College as to priority in removal of the parotid gland. We quote:

"In 1832, Dr. William Gibson, professor of surgery in the University of Pennsylvania, in a lecture delivered late in the year, denied that the parotid gland had ever been extir-

From the University of Texas, Medical Branch.

Presented in the symposium, The Salivary Gland, before the Clinical Congress of the American College of Surgeons, Boston, November 3–7, 1941.

TABLE I.—DISTRIBUTION OF 65 SALIVARY TUMORS

	Parotid gland		Submaxillary gland		Palate		Gum		Lacrimal	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
58 Primary salivary tumors	45	77.6	9	15.5	2	3.4	1	1.7	1	1.7
43 Mixed tumors	32	74.4	7	16.3	2	4.65	1	2.3	1	2.3
15 Malignant tumors	13	86.6	2	13.3						
7 Metastatic tumors	3 carcinomas 1 melanoma		2 carcinomas 1 melanoma							

pated. . . . The founder of Jefferson, Dr. George McClellan, had already reported several cases of extirpation of the parotid and this surgical triumph had been set up as one of the household gods of the Jefferson student body. The letter to Professor Pattison was dated January 1, 1833, and concludes:

"'We, the students of Jefferson Medical College, feeling the honour of our Professor (McClellan) involved, and the credit of our Institution concerned, in the fact being fully established, would feel obliged to you, if you would enter into a discussion of the question, *Has the Parotid Gland ever been extirpated?*'"

"John Bell (in his *Anatomy*) said: 'The cutting out completely of the parotid gland is a thing quite impossible, since the greatest of all the arteries, viz., the temporal and the maxillary, lie absolutely imbedded in the gland.'

"John Bell later revised his original doctrine in his treatise on surgery, stating that he had often extirpated the diseased parotid and his brother Sir Charles Bell says that he had assisted John in the extirpation of the gland"(1).

McClellan performed the operation successfully a number of times. Agnew recorded that Warren removed the parotid gland first in 1798 and McClellan's first case was in 1805.

The long interest in the mixed tumors has not been because of a high mortality from disease but from the fact that the embryology and pathology are without a satisfactory explanation and also because the treatment of them is still unsolved in spite of persistent effort on the part of the pathologist, the surgeon, and recently the roentgenologist.

The mixed tumors are defined by Harvey, Dawson, and Innes as "adenomas of the serous and seromucous salivary or lacrimal glands, of undifferentiated and gland-lobular types, which are very prone to a species of mucoid autolytic self-destructive transformation of their component tissues and are seldom truly malignant."

Still, Swinton and Warren say,

"The frequent tendency of epithelial cells to take on a spindle form has also been used to explain the apparent mesenchymal structure of certain of the elements of the so called mixed tumors. There are, however, certain objections to the consideration of the mixed tumors as adenomas with peculiar stromal changes. Adenomas readily recognized as such are extremely rare in the salivary gland. Moreover, this particular type of change in the stroma is almost unknown in adenomas developing elsewhere. It seems peculiar that in this group of glands alone a peculiar stromal change should develop in the adenomas which arise from them. In the very few instances of the true adenomas which have been reported there is no suggestion of the structure seen in the mixed tumor.

"The concept of a true mixed tumor developing from embryonic tissue is far more appealing. Distinctly in favor of this is the not infrequent occurrence of mixed tumors in diverse localities, such as the hard palate, the tonsillar fossa, the soft palate, the cheek, or the gum."

These tumors were at first thought to be purely epithelial in origin. Virchow thought that the cartilage was formed by pieces of metaplasia from connective tissue, while Cohnheim considered it to be a remanant of the branchial arches which became displaced during fetal life. The endothelial theory set forth by Wartman has been abandoned, and the epithelial generally accepted, particularly since the investigations of Kennon and Fry.

The figures given by McFarland for the relative occurrence of mixed tumors are: parotid, 93.6 per cent; submaxillary, 6.1 per cent; and sublingual, 0.3 per cent. They probably represent an unselected distribution of tumor occurrence for the glands concerned. Harvey and his co-workers studied 316 mixed tumors, and the locality was given or evident in 275 of these cases; parotid gland, 230; submaxillary, 21; sublingual, 2; lip, 9; palate, 6; nose, 1; and lacrimal, 6.

An analytical report of the cases of salivary gland tumor treated in the John Sealy Hospital and a study and comparative review of these tumors and others which have found their way into the Surgical Pathology Museum of the Medical Department of the University of Texas is summarized in Table I.

Of the 58 tumors arising primarily in the salivary tissues, 43 or 74 per cent were mixed tumors, and 15 or 26 per cent were carcinomatous, as shown in Table II. The distribution of these tumors according to location is given in Table I. Forty-five tumors were in the parotid gland alone, and of these 13 were malignant.

Symptomatically, in the mixed tumors, pain or tenderness was noted in an occasional case. These

TABLE II.—COMPARISON STATISTICS

No. of tumors	Singleton and Duren 58	Swinton and Warren 67	Stein and Geschickter 241 (parotid)	McFarland 300	Houck 46	Patey 55	Total No. 766	Revised averages	
								Yr.	Per cent
Per cent malignancy in salivary tumors	25.8	12.5	17.4		40.5		412		20.4
Age at onset in years									
Mixed	31.5	33.3					122	32.4	
Malignant	52.3	56.2					122	54.2	
Preoperative duration in years									
Mixed	5.4	10.7	8				363	7.8	
Malignant	1.24	3.6	4				363	3.5	
Recurrence in mixed tumors including those recurrent when first seen—per cent	33.3	17.6		23.2		23.6	477		23.8
Recurrence in mixed tumors operated upon at John Sealy Hospital	8.7% (J. S. H.)	4.3% (Lahey Clinic)	12.8% (J. S. H.)				363		8.6

however, were usually in the cases of the recurrent or very large tumors. The malignant tumors commonly caused symptoms. More than one-half of the present 15 were associated with tenderness, pain, or facial paralysis. The pain was occasionally radiating. Fixation to surrounding tissues was commonly met with.

The average age at onset for all the primary tumors was 38.0 years. Of these, the mixed tumors averaged 31.5 years; and the malignant tumors, 52.3 years. The preoperative duration of the mixed tumors averaged 5.4 years, whereas the malignant tumors averaged 1.24 years. The sharp clinical differences comparable to the two histological groups is to be noted.

The recurrence rate of the 58 salivary tumors is divided into 2 groups: That rate which recurred after excision of the tumor both elsewhere and at John Sealy Hospital and that rate recurring in the cases of patients operated on at John Sealy Hospital only. The recurrence rate should be considered in this manner because many of the cases were recurrent when first seen at this hospital. These data are available in 45 cases. Of these, 34 were mixed tumors; 10 or 33 per cent recurred. Of these mixed tumors, 2 or 8.7 per cent recurred. One of the two recurrences among the mixed tumors occurred in an elderly woman. It was widely excised, but recurred in 6 months and after 1 year had reached large proportions. It was again widely excised. The case was followed for 1 year, at which time there had been no recurrence. This tumor showed an increased cellularity in the recurrent tumor. This, considered with the marked infiltrative character noted at operation, classifies this tumor as one of the most malignant of the mixed tumors.

There is considerable controversy over the rate of recurrence in relation to the size of these tumors. The cases on which sufficient data were available were computed with this in mind. McFarland, dividing his series into tumors up to a walnut in size and a walnut or larger in size, stated that 32 per cent of the former and 16 per cent of the latter recurred. Houck, however, noted 17 and 31 per cent recurrence rates, respectively. In our series, 13.3 per cent of the smaller and 40 per cent of the larger tumors recurred. These and Houck's findings are in direct variance with those of McFarland.

One explanation for the low recurrence rate, 8 per cent, of mixed tumors of patients operated upon by us at John Sealy Hospital was the practice of wide excision. This is reflected in the high rate of postoperative complications, that is, facial paralysis. Ten cases among the mixed tumors were complicated by permanent facial paralysis. Of these, 8 were total. Facial paralysis occurred in all but 2 of the carcinomatous parotid tumors operated on. Salivary fistulas rarely occurred. Two of the present series of cases were so complicated.

TREATMENT

The diagnosis of the mixed tumors of the salivary glands is usually possible by physical examination and a history of a long duration of the tumor. A mixed tumor may be found in various parts of the orofacial region. Occasionally they are found in the lip, palate, supramaxillary border, nose, bronchi, and lacrimal gland. When the tumors are found in these locations, the diagnoses may be suspected, but usually such is not the case until microscopic study reveals the identity of the tumors.

Two years ago we stated in a discussion of these tumors of the parotid gland(6):

"Though the surgical treatment of tumors in various parts of the body has been standardized, that pertaining to the parotid salivary gland tumors is still in confusion, with wide variations in the opinion of the profession as to the plan to follow. Recurrences are frequent and therefore malignancy cannot be denied, but because of the infrequency of distant metastasis and the anatomic difficulty of extensive surgery without facial nerve injury, incomplete or local operations are the rule. Investigation will reveal that the early experience of the surgeon will show a strenuous effort to preserve the nerve, but with more experience and increasing number of recurrences, a more radical procedure is preferred with less regard for the nerve. Such has been our experience in dealing with the parotid tumors."

We also advocated radical surgery for carcinoma of the parotid gland, stating,

"Because of the uncertainty of prognosis the frankly malignant tumors are usually treated conservatively to save the facial nerve. Therefore, we believe that conservative surgery is responsible for the high percentage of the recurrences, both in the mixed and malignant tumors. For some years we have felt that we were justified in removing large amounts of the parotid gland and even all the gland in those cases where we were convinced that sacrificing the facial nerve was necessary for a cure"(6).

To justify radical removal of mixed tumors because of their possible transformation into carcinoma or sarcoma is questioned by good authorities. A few cases have been reported in which such a transformation has occurred, but they are rare. In 1 of our cases this seemed undeniable, but investigation of case histories does not justify this as a reason for radical surgery. One of the most incurable malignant tumors we have found is carcinoma of the parotid gland. Even with the most radical surgery early in the course of its growth, only a very few cures are on record. We have not seen one patient who has lived 5 years after treatment. This includes 15 definitely proved carcinomas of the parotid gland which we have operated upon in a radical way. Three of these are still free of recurrence, but a 5 year period has not yet elapsed in any one of these. McFarland reported 14 cases of carcinoma of the parotid gland, 1 of questionable diagnosis, and only 2 patients were alive 5 years and these had multiple operations for recurrence.

In the case of mixed tumors of the parotid, McFarland argues against removal when they are small, claiming that the recurrences are more likely in the small tumors. This is not the experience of others, including ourselves.

It requires tremendous restraint on the part of the surgeon to allow an ever prominent parotid tumor to be turned away without removal. In no other large group of tumors is the attitude of conservatism considered, but the all important complication, facial nerve palsy, which must follow radical surgery in this region, is responsible for unsatisfactory results after their treatment. Unless it becomes large, the tumor is preferable to a facial palsy. Many plastic procedures are used to counteract this distressing complication, some of which are satisfactory to a marked degree, but they are far short of completely correcting the deformity. The result appears satisfactory at first, but, unfortunately, due to atrophy of muscles the deformity becomes more marked with the passage of time after most plastic procedures.

At the present time we have under observation a nurse who has a parotid tumor deep in the parotid gland directly in the path of the facial nerve. The tumor is not growing rapidly, and, since a facial palsy would put an end to her profession as a nurse, upon which she depends for her livelihood, I cannot to this time make up my mind to disturb it. McFarland's persistent and careful clinical study of a very large series of parotid tumors resulting in the conclusion that conservatism should be emphasized in their treatment, cannot be entirely disregarded. We would emphasize that every effort should be made to save the facial nerve, at least in the initial attempt at removal. A planned sacrifice of the facial nerve is justifiable in cases of recurrence and in carcinoma. Plastic repair is of great importance but does not prevent an objectionable deformity of the face.

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THE SULFONAMIDE DRUGS IN THE TREATMENT OF ACUTE SUPPURATIONS IN THE MIDDLE EAR AND MASTOID

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THE sulfonamide drugs met with prompt and enthusiastic acceptance in the field of otolaryngology where there remained many unsolved problems of coccal infections. The acceptance of these preparations was characterized at first by overenthusiasm and favorable prejudice. Although they have found a permanent place as some of the most valuable therapeutic agents in the otologists' armamentarium, they must not at once supplant other forms of treatment of proved worth.

One of the most controversial subjects referable to the use of these preparations is that pertaining to their efficacy in the treatment of acute suppurative otitis media and mastoiditis. Most otologists are willing to admit that since the use of sulfanilamide and sulfathiazole the incidence of surgical mastoiditis, the complications of acute suppurative otitis media and mastoiditis, and the mortality rate dependent upon these conditions have been diminished greatly.

Kolmer has said that "chemotherapy is not merely the treatment of a disease with chemical agents; that is as old as the art of medicine itself. Rather it is the treatment of disease produced by living pathogenic organisms with specific chemical agents or drugs capable of selectively destroying them without serious toxic effects." When a drug is found to be efficacious in the treatment of one type of infection, it does not necessarily follow that it will be of equal benefit in all infections. Yet such a discovery is prone to bring about indiscriminate and empirical use of the compound. This has happened to a great extent in the case of the sulfonamide drugs.

The new chemotherapeutic agents are not devoid of dangers in their administration and their usage should be governed by the results of careful investigation of the patient and the disease to be treated. First, one must weigh the possible benefit to be derived from treatment, against the dangers of administration of the drug.

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In reference to acute suppurations in the middle ear and mastoid the following points must be considered. First, the oral administration of the chemotherapeutic drugs in acute suppurative otitis media and acute mastoiditis, and, second, the local use of the drugs in mastoidectomy wounds.

In the case of acute suppurative otitis media, the first question that must be answered is "which patients with this disease need chemotherapy?" It has been conceded by many otolaryngologists that over 90 per cent of cases of acute suppurative otitis media proceed to spontaneous resolution after an adequate and timely myringotomy. Now since the advent of the sulfonamide drugs most encouraging reports relating the marked decrease in the morbidity from acute suppurative otitis media and the reduction in the number of cases of surgical mastoiditis have appeared. Stuart, Bowers, Clein, Lindsay, Horan and French, Baker and Bradford, Galloway, and others have reported favorably on the treatment of acute suppurative diseases in the middle ear and mastoid by the use of these compounds. Long (12) has even suggested that chemotherapy might be used for 48 to 72 hours at the very beginning of an earache in an effort to prevent the development of a suppurative otitis media. Williams and his co-workers concluded that chemotherapy afforded the greatest protection against surgical mastoiditis when used in otitis media due to pneumococci. Osgood on the other hand advised against the use of chemotherapeutic drugs in conditions in which there is little or no mortality rate, and Lindsay emphasized the statement that "the treatment for a patient who is desperately ill is not necessarily a criterion of the best policy in the early stages of these infections or in a moderate or mild type of otitic suppuration."

Babcock seemed unwilling to admit that the decrease in the number of surgical cases of mastoiditis in New York was due solely to chemotherapy, and he indicated that the effect of this treatment in otitis media is somewhat overrated.

Before subscribing to the practice of giving chemotherapy to every patient suffering from acute otitis media, one should analyze some of the

extremely favorable reports of drug therapy. It seems that reported reductions in the number of cases of surgical mastoiditis may be somewhat misleading, since many of the reported controlled groups demonstrate an extremely high percentage of cases of surgical mastoiditis. Let us attempt to determine possible causes for the fewer cases of surgical mastoiditis other than the direct effect of the sulfonamide drugs upon middle ear infections. Kopetzky has reported a distinct periodicity in the virulence of infection of the upper respiratory tract, particularly of the middle ear and mastoid, and has stated that in different years various substrains of the hemolytic streptococcus may be predominant. He suggested that a major cycle occurred about every 6 years.

Since chemotherapy has come to be used in a large number of patients with exudative nasopharyngitis, severe follicular tonsillitis and suppurative sinusitis with excellent results, many severe acute cases of suppurative otitis media probably have been prevented. This in itself has tended to reduce the number of surgical cases because these fulminating infections that spread to the middle ear, eventuate in suppurative mastoiditis with relatively great frequency. Then there was that group of otolaryngologists who were prone to operate early in every case of severe otitis media which demonstrated fever, pain, profuse discharge, and mastoid tenderness. The more conservative aural surgeons had the courage to postpone surgical interference upon patients who demonstrated signs of uncomplicated mastoiditis in the first week of infection in the middle ear. This delay provided time for spontaneous resolution in the majority of patients and allowed walling off of the process in those who continued to develop a suppurative coalescent process in the temporal bone. Since the widespread use of chemotherapeutic agents in middle ear infections these early operations of which we know there was a tremendous number, have been reduced to a minimum for the following reasons: First, the prevention of otherwise necessary operations due to the effect of the drug in the severe cases of acute suppurative otitis media. Here the acute infection in the middle ear was brought under control before extension to the mastoid had taken place. Second, and the exact importance of this factor cannot be determined, the prevention of unnecessary operations. The confidence in the sulfonamide drugs possessed by the patient, the general practitioner, the pediatrician, and the otologist, has acted as a deterrent to operation. The tempering of the acute symptoms has made the condition less alarming so that there has been no impatient cry for action on the part of the patient, parents, or physician and many cases have been allowed to proceed to spontaneous resolution which might have taken the same course without the drug if sound, watchful conservatism had been practiced.

Now, since prompt and excellent response to chemotherapy in severe acute cases of suppurative otitis media has been witnessed, why should not all cases of middle ear infection be treated routinely by the administration of one of the sulfonamide drugs? In answer to this question I wish to state that chemotherapy should be used scientifically and specifically with a definite objective in view. There is a morbidity and even a mortality rate attendant upon the use of these weapons which must not be ignored. If the object is the prevention of mastoiditis we are then considering a form of treatment which should not be given to over 90 patients unnecessarily in order to treat less than 10 who need it. Even though the drug were perfectly innocuous, such empiricism does not belong to the present era of scientific medicine. If the object is, and of course it should be where possible, to decrease the morbidity and to shorten the duration of the infection then a much higher percentage of patients with acute suppurative otitis media may be treated by these drugs. They should be selected on the basis of their general condition and the severity of the infection but should not be subjected to routine empirical treatment. The patient who has an infection severe enough to demand chemotherapy should be kept under close observation in order that the effect of the drug on the infection may be observed and the earliest signs of toxic reaction be detected. Those adult patients with mild acute suppurative otitis media treated by chemotherapy often insist upon remaining ambulatory and driving automobiles. The dangers attendant upon this are well known.

Finally the very significant number of patients who develop mastoiditis and intracranial complications insidiously during chemotherapy adds a new note of danger. The masking effect of the drug which allows these complications to develop without any alarming signs tends to give the physician a false impression of the patient's progress.

Allowing the sulfonamide drugs their very important place in the treatment of acute suppurative otitis media, which patients then with this disease should receive their benefits? Although it is difficult to draw any hard and fast rules, a few principles seem worth while to follow.

This treatment is best suited to those individuals in whom the disease is still a mucous mem-

brane infection, and of course to those who have established and diagnosed complications of the suppurative process in the temporal bone. Bearing this in mind, chemotherapy should be used in the following types of cases:

1. Acute fulminating infections in the middle ear producing signs of mastoid involvement at the end of the second or third day and characterized by sepsis, profuse aural discharge, pain and mastoid tenderness. In this type of disease there is frequently a spread of the infection by septic thrombophlebitis of the small communicating veins of the mastoid.

2. Acute infections in the middle ear, either mild or severe, but secondary to a virulent process in the throat, nasopharynx, nose or paranasal sinuses. Chemotherapy in these cases may prevent a suppurative mastoiditis by controlling the primary infection.

3. Early, acute, rapidly developing middle ear suppurations characterized by a red edematous tympanic membrane and thin seropurulent or serosanguineous exudate under pressure in the tympanum. This is the type of infection which may spread rapidly to the mastoid if not brought under control promptly.

4. All cases of acute suppurative otitis media from which a pneumococcus is recovered on culture.

In general only those patients who have an early acute suppurative otitis media without an established suppurative mastoiditis gain the greatest therapeutic effects from the drug. If suppurative mastoiditis has already developed, treatment will be less effective. Williams stated that "on the basis of review of literature in consideration of the mode of action of the drug, it would seem that the sulfonamide drugs act best in an environment in which good blood and oxygen supply are present, one which is free of peptones and broken down leucocytes and which is not constituted of bone. The middle ear and mastoid process are essentially bony loci with a notably poor blood supply." The condition in an infected mastoid is entirely different from that in an acute osteomyelitic process in the vascular red marrow of the metaphysis of a long bone. In the latter infections chemotherapy has started to revolutionize their treatment. Badgley reported 13 cases of acute osteomyelitis in the long bones treated by sulfathiazole. In each of 3 patients incision and drainage of soft tissues only was done and in 10 patients no incisions at all were made. All of these patients made splendid recoveries. With continued chemotherapy most otologists have witnessed infection in the mastoid proceed to intracranial involvement. Although one might offer as an explanation the difference in the types of bone in the mastoid and in the long bones, it has been our experience at the University of Michigan Hospital that spreading osteomyelitis of the skull, an infection in diploic bone, is not satisfactorily managed by chemotherapy alone. We still find it necessary to remove all infected bone and to expose a wide margin of healthy dura around the osteomyelitic process.

When sulfanilamide was the only sulfonamide drug available, it was usually advisable to know what organism was responsible for the infection before instituting therapy. This was due to the toxicity and the somewhat limited effectiveness of the preparation. Culture of the infecting organisms is still important and should be performed in every disease in which chemotherapy is contemplated; yet the newer drugs with wider scope of action and decreased toxic effects may be started before the culture has been completed. At the present time sulfathiazole is the drug of choice in most instances because of its effectiveness in combating infections due to hemolytic streptococci, pneumococci, and staphylococci. Sulfadiazine which is now available, but rather expensive, bids fair to replace sulfathiazole as the preparation of choice in most of the infections encountered in an otolaryngologic practice. Long (13) has commented on the low toxicity of sulfadiazine and has stated that it is the only one of the group of the sulfonamide drugs that can be used in the home with relative safety.

The period of time during which chemotherapy should be employed in infections of the middle ear and mastoid has been the subject of controversial discussion. Bowers, Kolmer, Osgood, Lyons, Lindsay, and Williams, have dealt with the subject in some detail. Although it has been suggested by some that it might be advisable to wait for a few days after the infection appears in order to allow antibodies to develop before giving the drug, the general opinion now seems to be that treatment should be started immediately upon the appearance of the infection and that the dosage should be very heavy during the first day in order to gain a high blood level of the drug as soon as possible. Of course by the time a severe infection becomes manifest antibodies have already been produced to a considerable extent.

Since the greatest effect of the drug is to be gained when the infection is in the mucous membrane, or when there is being produced a septic thrombophlebitis of the small communicating vessels of the temporal bone, such therapy should be used during this period and then discontinued until further indications for its use arise. This

means that treatment should be given vigorously for 4 to 10 days, at the end of which time it has probably had its complete effect upon the early stage of the infection. Earlier discontinuance is indicated, of course, if important toxic manifestations appear. Failure of the infection to respond to therapy may indicate a lack of antibodies which should be supplied by transfusions or specific sera if available.

The indications for use of chemotherapy in the early stages of severe acute suppurative otitis media are more easily defined than are the indications in infections of the middle ear and mastoid of more than a week or 10 days' duration. Empiricism must again be avoided in the latter group of cases and the drug should be used only after full consideration of each individual case. Although fever may be lessened and the objective signs of manifest bone involvement within the mastoid may be partially alleviated, the disease within the temporal bone is not likely to undergo spontaneous resolution at this stage if the patient is ill enough to demand chemotherapy. Because of the masking effect of the drug which may be due, as suggested by Lindsay, to a limitation of the infectious process, the otologist may be confronted by the insidious development of an intracranial complication.

Coalescent mastoiditis can and does proceed to develop on many occasions during intensive chemotherapy. Since this may happen rather quietly an especially alert vigilance must be maintained. Signs of the surgical mastoid are almost always present but are modified due to the lack of fever, pain, severe tenderness, and leucocytosis. The characteristic granular purulent exudate, sagging of the supraposterior canal wall, deafness, and progressive radiographic changes are present in most instances but are less imperative.

The local use of the sulfonamide drugs in infected and potentially infected wounds has been given a thorough trial in civilian and military surgery and has been proved to be of great value.

The postoperative care of mastoid wounds has changed from time to time in an effort to shorten the time of healing and yet assure adequate drainage. Many procedures varying from wide open drainage to primary suture after allowing the cavity to fill with blood clot have been suggested. More recently otologists have been using the sulfonamide drugs in the mastoid cavity in addition to regular gauze or rubber drains. Livingston had disappointing results from filling the mastoid wound with sulfanilamide crystals and then using the usual rubber drain and partial suture and believed that this procedure failed to shorten the postoperative period. He reported 13 cases in which the wound was filled with either sulfanilamide or sulfathiazole and then closed tightly, of which 11 showed prompt healing. Of the 11 patients so treated, the shortest healing time was 4 days and the longest healing time 9 days.

At the University of Michigan Hospital observations have been made by Dr. David DeWeese on 10 simple mastoidectomy wounds treated by the local application of sulfanilamide powder at the time of operation. The wounds were nearly filled with the powder and then the usual gauze packing was inserted. Wound cultures remained negative for streptococci until after the first dressing was done on the fourth or fifth day, when streptococci and staphylococci began to appear. In 8 of the 10 wounds, no pus was seen until after the packing had been changed. The highest blood sulfanilamide level obtained was 0.45 milligrams per cent following the instillation of 10 grams of drug in the mastoid wound. The next highest blood level was 0.2 milligrams per cent and the remainder showed a very small amount of the drug in the blood. Although no conclusions can be drawn from this small group of cases, it seems certain that the effect of the drug upon the wound must be local and not the result of absorption. Also it might suggest that the wounds were reinfected in dressing them in spite of the fact that aseptic technique was employed in the procedure. Reinfection of the wound at the time of dressing is not the only explanation of the postoperative suppuration although this factor is important when any wound is dressed frequently. After a well done complete mastoidectomy, there remain many small infected cells which may account for the reappearance of pus after the fifth postoperative day. Since some of these infected cells do remain it would seem that primary suture of the complete mastoid wound after the local use of the sulfonamide drugs is not an entirely safe procedure, because provision is not made for open drainage. The local use of the drug, partial suture of the wound, and the use of a rubber drain that can be removed gradually without having to be reinserted probably offers the best type of dressing for the average complete mastoidectomy wound.

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RESULTS OF OPERATION FOR HETEROPHORIA AND HETEROTROPIA AND CAUSES OF FAILURE

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THE subject of heterophoria and heterotropia may be discussed from several viewpoints. I have chosen to discuss it in relation to the type of operation indicated or contraindicated according to the diagnosis. There may be some who do not yet think of squints and phorias as having *definite* surgical indications, depending upon an accurate diagnosis.

The subject of diagnosis has already been discussed by my distinguished colleague Dr. White.

THE HETEROPHORIAS

The heterophorias may be divided into the esophorias and the exophorias. The esophorias may be mechanical, accommodative, or mechanical plus accommodative; the mechanical or essential esophoria may be due to convergence excess or to divergence insufficiency.

Essential esophoria due to convergence excess is curable by surgery; it may possibly be symptomatically alleviated by other means but not cured. When due to convergence excess a lessening of the action of the median rectus or recti will result in a permanent cure. If it be due to divergence insufficiency, operation upon the median rectus will not only fail to relieve the esophoria but will permanently disable the convergence and the condition will be worse than before. We have found the Jameson recession operation to be eminently satisfactory, only one median rectus being recessed at a time.

The cure of this form of esophoria may be achieved only by proper surgery. It may require a procedure as extended as that for the cure of convergent squint of the same type. A lapse of some months should be allowed after the first operation before an operation is done upon the median rectus of the fellow eye, should this be necessary.

In mechanical esophoria due to divergence insufficiency shortening of one or both lateral recti will result in a permanent cure. Obviously, the extent of the shortening wll depend upon the degree of the esophoria. Careful study and understanding of the case enables the surgeon to judge as to the extent of the operation. When properly performed as to surgical technique and with a full understanding of the surgical requirements in the particular case at hand, the result will be eminently satisfactory in a very large majority of the cases. Naturally, no surgical procedure is satisfactory in all cases. In a case of esophoria due to divergence insufficiency, operation upon the median recti is contraindicated.

It is unfortunate to put glasses upon a patient with mechanical esophoria since they have no effect whatever upon the degree of the esophoria. In a purely mechanical esophoria it will be obvious upon reflection that correction of the refraction will not alter the degree of the esophoria and hence will not relieve the patient. Only if there be an accommodative factor will the degree of the esophoria be lessened.

Regarding accommodative esophoria, or functional esophoria, I wish to emphasize the following statement. In purely accommodative esophoria, surgery is absolutely contraindicated. If operation is done, the result will be an exophoria for distance and an esophoria for near. The esophoria will probably develop into a divergent squint for distance with an esophoria for near.

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It is improper to prescribe glasses for permanent wear. They do not cure an accommodative esophoria but correct it only while the glasses are being worn. This is symptomatic treatment only and is unscientific. Accommodative esophoria can be cured by dissociation of the accommodation and convergence by proper orthoptic training.

In combined mechanical and accommodative esophoria, the mechanical factor requires surgical correction according to the suggestions made. The accommodative factor is amenable to orthoptic training as mentioned. An accurate diagnosis before treatment is attempted is essential.

The exophorias may be mechanical, accommodative, or mechanical and accommodative; in mechanical exophoria due to convergence insufficiency surgery is necessary. Proper correction of the myopia, together with orthoptic training to correct (1) the convergence insufficiency, (2) to improve fusion to a wide amplitude, and (3) to obtain third degree fusion or stereopsis, may give satisfactory functional results but will not cure the exophoria.

To obtain a permanent cure, shortening of the median rectus or recti is indicated. The results are not so satisfactory as in esophoria. Relapses are more frequent. Judgment is more difficult as to the degree of shortening indicated. A primary overcorrection is desirable.

The results are often not entirely satisfactory. Bielschowsky suggests it is better to wait until adolescence before operating in such cases. Our experience justifies this. Careful study of the patient, patience, and an understanding of the many factors involved will enable the surgeon, with proper surgical measures, to obtain a satisfactory cure in the majority of cases.

It is my impression that, in the presence of mechanical exophoria due to divergence excess, more brilliant successes are obtained by means of surgical treatment in this condition than in any other motor anomaly of the eyes.

Lessening the action of one lateral rectus at a sitting followed by a similar procedure on the fellow eye after the proper interval of time has elapsed results in a permanent cure more certain than does that secured by any other surgical procedure. The Jameson technique, recessing one lateral rectus 4 to 5 millimeters, appears to us to be the ideal operation. It is unsafe to recess both at one sitting, and it should not be done.

Exophoria of more than 8 prism diopters for distance prevents entrance of a recruit into the commissioned personnel of the armed services, the air corps, or commercial flying. The surgical cure is so easy and so eminently satisfactory that no person should be deprived of the inestimable benefit of correction. In selected cases and under proper conditions, the patient will not have to remain in the hospital but may resume his duties within 24 hours.

Mechanical plus accommodative exophoria is usually an exotropia and will be discussed under that heading.

Accommodative exophoria is the result of myopia. The myope of 2 or 3 diopters or more uses no accommodation for near work and hence little or no convergence. In consequence such a patient develops an exophoria which very soon becomes an intermittent exotropia at which time there begins to develop a mechanical factor.

A purely accommodative exophoria does not indicate surgery; cure can be obtained by correction of the refraction and orthoptic training.

SQUINT

Squint may be convergent or divergent.

Convergent squint may be (1) mechanical (a) due to convergence excess, (b) due to divergence insufficiency, (c) due to convergence excess plus divergence insufficiency; (2) accommodative; or (3) mechanical plus accommodative.

Divergent squint may be (1) mechanical (a) due to convergence insufficiency, (b) due to divergence excess, (c) due to convergence insufficiency and divergence excess; (2) accommodative; (3) mechanical plus accommodative.

Convergent mechanical squint due to convergence excess is not benefited by glasses. Orthoptic exercises alone will not correct the squint; if it does so the squint is not a mechanical one. Surgical treatment is indicated and should aim to lessen the action of the median rectus or recti. In this form of squint we have found that the Jameson recession operation, properly used, gives eminently satisfactory results. To secure a functional cure in such cases, 3 factors are necessary: (1) absolutely accurate diagnosis; (2) knowledge of how much to recess the median rectus or recti; (3) efficient orthoptic training to secure fusional amplitude and stereopsis. The causes of failure are obvious, the most important of which are incorrect diagnosis and consequent improper surgery; uncalled for or an improper surgical procedure will result in failure. Shortening or advancement of the lateral rectus or recti is contraindicated and will result in an unsatisfactory result or failure.

The surgical treatment in mechanical convergent squint due to divergence insufficiency should be directed to the lateral recti. We seek to in-

crease their action by advancing, shortening, or both, by any operative procedure the surgeon prefers or in which he is most adept. The particular operation is of no great moment, but the choice of operation is essential to success. Error in this choice will cause failure, partially or completely. To operate upon the convergence muscular system when the divergence only is involved, will cause tragic failure since the squint will not be relieved and the convergence will be weakened. This adds to the cosmetic failure, a weakened convergence which may cause great trouble.

Surgery is absolutely contraindicated in purely accommodative convergent squint. Cure can be secured in such cases only by orthoptic training. If operation is done there will be a divergent squint for distance. The result of surgery in such cases is tragic failure and renders such eyes absolutely incurable for all time.

In accommodative mechanical convergent squint the mechanical factor should be corrected by surgical means; the accommodative, by orthoptic training. Before operation is done to correct the mechanical factor, due regard should be given to the question whether the squint is the result of convergence excess or divergence insufficiency as above discussed. Failure to observe this or failure to recognize the accommodative element will bring about unsatisfactory results.

In cases of mechanical divergent squint it is unusual to find a patient without an accommodative factor; the majority have myopia. Bielschowsky advised that no operation be done to correct divergent squint before the adolescent age because of the possibility of recurrence. This judgment was no doubt formed in Germany. In our country conditions are so different that this would not seem to be proper judgment here. Because of the adverse effect on the mental development of a child, any squint should be corrected and cured at the earliest possible moment.

Mechanical divergent squint requires surgery for a cure in the following instances:

a. When due entirely to convergence insufficiency shortening of the median rectus or recti is necessary. Considerable experience is necessary in order to determine the degree of shortening or advancement or both that may be required. When combined with orthoptic training to overcome suppression, which is almost always present, the results are good. Recession of the lateral rectus or recti may be necessary in high degrees of divergence in addition to shortening of the median rectus. Overcorrection is required since there is a strong tendency for the squint to recur. In our experience correction of a mechanical divergent squint is more difficult and less satisfactory than that of convergent squint. The patient should be informed that recurrence may occur and that further surgery may be required. Suppression which is likely to be intermittent is difficult to overcome, consequently extended orthoptic training may be required and the case kept under observation over a long period.

b. Surgery is necessary in mechanical divergent squint due entirely to divergence excess. One rarely finds such a case. Often exophoria is due purely to divergence excess but by the time it has become an exotropia there is usually added convergence insufficiency. In a case with pure divergence excess, recession of one or both recti gives a most satisfactory cure which is often permanent, provided there is no convergence insufficiency or the anatomical anomaly is not so great that recurrence is likely. Obviously orthoptic training and correction of the refraction are concomitant necessities in obtaining a cure. May I emphasize the word *cure* which means binocular vision with stereopsis. Without this the case is only cosmetically corrected not cured.

In the great majority of cases of divergent squint due to divergence excess plus convergence insufficiency, a high degree of resection and advancement of both median recti may be required, possibly combined with recession of the lateral recti. A cure is not always possible though a cosmetic correction may be secured The advanced muscle detracts from the cosmetic result. Limitation of abduction may result even though both eyes are operated upon. This is undesirable but may be necessary in correction of ocular deformity.

The causes of failure of correction appear frequently to be an insufficient degree of resection and advancement primarily to overcorrect the squint. Extreme limitation of movement of one eye may result from too great shortening of the median rectus with or without recession of the lateral rectus. The correction necessary in the higher degrees of squint should be equally distributed between the two eyes. An excess correction may result in convergent squint which may cause an annoying and possibly an insuperable diplopia. One should proceed with caution in high degrees of alternating divergent squint. Correction of the deformity may result in diplopia, so annoying to the patient that it cannot be endured. We believe such cases to be very rare and have not hesitated to correct such squints. We have had no case of serious diplopia following surgical correction.

Accommodative divergent squint differs in many respects from accommodative convergent

squint. It is the beginning of the mechanical form and results from myopia. The child is myopic and uses no accommodation for near vision consequently no convergence. He fixes with one eye and the other is relatively divergent. Hence suppression occurs for near vision which is therefore intermittent suppression. Slight amblyopia may occur which later becomes more marked as the squint progresses from an intermittent to a continuous one.

The child has a divergent squint only for near at the beginning, hence it is functional i.e. accommodative. The child, however, only squints when he is looking down, that is, in near work. Consequently, it is not observed by the parents. Very likely his myopia will not be discovered until he goes to school. By this time the squint will probably have a mechanical factor in addition to the accommodative factor.

It is obvious that we rarely see a purely accommodative divergent squint. It is equally obvious that surgery is not indicated if the case be entirely accommodative. Correction of the refraction and orthoptic training will be adequate to establish a cure in such a case.

In mechanical plus accommodative squint surgical correction and in addition orthoptic training and correction of the refraction are required. Surgery properly adapted to the particular case is usually satisfactory and a cure is accomplished in conjunction with the other treatment mentioned. The degree of squint is usually not great and there should be no failures in such cases. Failure could come only from improper diagnosis and poorly conceived or improperly performed surgery.

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OTOLOGICAL SYMPTOMS OR COMPLICATIONS OF CRANIOCEREBRAL INJURY

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WITH the accelerated pace of our industrial life and with war rampant in the world, there are an ever increasing number of head injuries. With the exception of headache, the most frequently encountered symptoms of head trauma lie in the field of otology.

The anatomical considerations are briefly these: the external ear, external canal and membrana tympani; the middle ear; the cochlea and vestibule; the cochlear and vestibular nerves; the facial nerve; the first way stations of cochlear and vestibular nerves in the floor of the fourth ventricle and brain stem; and the central cochlear and vestibular connections.

In the production of intracranial damage the head may strike an object, be struck by an object or be violently jarred against the vertebral column. In considering the mechanics of such an injury there are three distinct phases: (1) the moment of impact; (2) the movement of skull and brain; (3) the cessation of skull movement. As the brain floats freely in the cerebrospinal fluid and as there is a certain element of inertia in its movement, it can be damaged by impact against the inside of the skull in either the first or the third phase of the injury. Such damage, when it occurs in the third phase, is of the contre coup variety.

As to the type of pathology produced, there may be fractures of the skull with concomitant brain injury or brain injury without any demonstrable skull fracture. Fractures of the skull may involve the facial bones, the vault, the base, or any combination of these. Fractures of the base constitute from 60 to 80 per cent of all skull fractures. They may involve the anterior, middle or posterior fossae, but those involving the middle fossa predominate. They may be of the bending or bursting type.

Fractures of the temporal bone, which is very loosely fitted into the base and which constitutes a large portion of the middle fossa, occur whenever the middle fossa is fractured. Transverse fractures of the temporal bone, which cross it more or less at right angles and destroy its contents, are initiated in the posterior fossa. The contents of the temporal bone may also be damaged by violent swinging movements of the temporal bone without any fracture having taken place. In the vast majority of cases, a transverse fracture of the temporal bone causes a complete cochleovestibular paralysis, but there are a few well authenticated cases in which a portion of either the cochlear or the vestibular function is spared.

Another type of injury of interest to the otologist is injury to brain tissue, particularly pathology involving the brain stem and the region of the floor of the fourth ventricle where it can damage the cochlear and vestibular nuclei and their central connections. Such pathology consists of contusions and petechial hemorrhages; the tearing of blood vessels; the tearing, stretching, and laceration of cranial nerves; and damage to the vasomotor center and vasomotor nerves resulting in irritation of the vestibular nuclei.

A third type of injury which is of peculiar interest to the otologist is the direct injury to the cochlear and vestibular end organ. This is occasioned by transverse fractures of the otic capsule which actually destroy the sensory epithelium, by longitudinal fractures of the temporal bone which do not of themselves invade the capsule but which are associated with bleeding into the basal coil of the cochlea, by the tearing or stretching of the eighth nerve at the internal auditory meatus and by wave movements of perilymph and endolymph caused by violent swinging movements of the entire pyramid.

Careful history taking is of importance in evaluating a head injury. In general it may be said the older the patient the more serious are the effects of the injury and vice versa. The baby's skull, because of its great elasticity, absorbs the effects of trauma very well. The question of unconsciousness is an interesting one. In general it may be said that the longer the period of unconsciousness the more serious the injury. And yet, we encounter rather serious intracranial damage in cases in which no loss of consciousness occurred. A truck driver walked into my office a few weeks ago complaining of headache. Ten days before, while closing the rear doors of his truck he fell

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backward, striking his head against the pavement. He continued his work as a truck driver until he consulted me. Examination revealed a linear fracture of the occipital bone about 4 centimeters long. At no time was he unconscious.

Bleeding from the mouth, nose, or ears generally indicates a basal fracture. It may come on immediately, but in some cases it may be delayed for a couple of days or even up to a 2 week period. The history of any previous injury to the head is of value in evaluating the signs. Any information as to the previous condition of the cochlear or vestibular apparatus is of vital importance.

In the examination of the patient, the importance of team work between the surgeon, neurologist, ophthalmologist, and otolaryngologist cannot be stressed too strongly. Otological examination divides itself into immediate, as soon after injury as possible, and subsequent examinations.

The immediate examination of the patient should concern itself with the following points: presence or absence of consciousness; presence or absence of facial paralysis or weakness; presence or absence of ptosis or strabismus; condition of the pupils and pupillary reflexes. The otoscopic examination will disclose any blood or cerebrospinal fluid in the external canal, any bloody crusts, fissures or cracks in the canal wall, any rupture of the drum or the presence of hematotympanum. Rough hearing tests should be made as soon as the sensorium of the patient permits to determine qualitatively if hearing is present. The presence or absence of spontaneous nystagmus in different positions of the eyes should be noted, especially if there is a complaint of dizziness. If the patient is unconscious, a conjugate deviation of the eyes can often be seen. This has the same significance as a spontaneous nystagmus in the conscious patient.

Subsequent examinations will concern themselves with a study of all the cranial nerves. The sense of smell should be investigated. The eyes should be studied in regard to pupil size and reaction, action of the extraocular muscles, media and fundi, diplopia and the field of vision. The action of the facial nerve should be carefully investigated. The hearing function should be examined by the voice, tuning fork reactions, and the audiometer, preferably in a sound proof room. A study of the vestibular mechanism should include all the spontaneous signs of vestibular disturbance as well as the induced vestibular reactions, both thermal and rotatory.

SIGNS AND SYMPTOMS

The signs and symptoms which especially concern the otologist are tinnitus, loss of hearing, dizziness, the escape of blood or cerebrospinal fluid from the ear, the presence of facial paralysis or weakness, the presence of fracture lines in the external auditory canal, and the development in 4 to 5 days of Battle's sign, ecchymosis over the mastoid process.

Spontaneous vestibular vertigo is subdivided into turning or rotatory vertigo and tactile vertigo. In turning vertigo the patient will indicate in some way that either he feels himself turning, the more common variety, or that objects in his environment are rotating, not so common. There is no more certain sign of vestibular disturbance than turning vertigo. Tactile vertigo is again divided into: (1) errors of sensation and (2) lateropulsion. In lateropulsion, which is not very common, the patient feels himself being pushed to one side.

The patient with an error of sensation has a feeling of tilting or tipping, of uncertainty or unsteadiness, or he complains of faintness or spots before his eyes. He does not experience any sense of rotation. His vertigo is not accompanied by spontaneous nystagmus, but his vestibular mechanisms usually show unequal responses to thermal stimulation.

Unless there has been a complete cochleovestibular paralysis caused by a labyrinthine fracture, the vertigo is not constant but comes on in bouts initiated by sudden movements of the head, bending, lifting, exposure to sun and heat, elevation above ground level and indulgence in alcohol.

The spontaneous signs of vestibular disturbance are of more importance in checking for brain stem pathology than are the induced reactions, induced by either the caloric test or the rotation chair. These spontaneous signs are nystagmus, past pointing, drift in the deviation test, gait deviations, the Romberg test, and the girdle reactions.

Spontaneous nystagmus due to vestibular disturbance is a jerky nystagmus. It is usually rotary and horizontal. If vertical or diagonal in character, it may be due to a brain stem lesion but it is not vestibular in origin. After a total exclusion of the labyrinth, it is continuous; but if due to pathology in the region of the vestibular nuclei, it is intermittent. It may appear in all three positions of the eyes, but if mild in degree, will only be seen if the eyes are turned in the direction of the quick component. It should be searched for in every position of the head and eyes; with the head erect, head tipped backward and then forward, and with the head tipped to either shoulder, the so-called positional nystagmus. If no nystagmus is seen in these positions, it can sometimes be made to appear by rapidly

shaking the head, the so-called "head movement test." This test will not produce a spontaneous nystagmus in a normal individual. If a spontaneous nystagmus is intermittent in character, do not expect to find it on every examination and do not make the mistake of saying that there is no spontaneous nystagmus present in a patient from one single examination. The nystagmus will only be present on those occasions when the central vestibular nuclei are being irritated and when the patient has a subjective sense of rotation. This also applies to the other spontaneous signs of vestibular disturbance.

If a patient has a subjective sense of rotation, he will past point when the pointing test is made in the vertical plane, his outstretched arms will drift to the right or left in the deviation test of Fischer and Wodak and he will deviate to one or the other side when he walks forward or backward with eyes closed.

If the patient has a sense that he is tipping or tilting, he may past point if the pointing test is made in the horizontal plane.

The falling reaction is best tested by the Romberg test. I shall not try to describe to you the technique of performing the Romberg test. Suffice it to say that when making the test in a medicolegal case, every effort should be made to divert the attention of the patient while the test is made. If a falling tendency is due to a peripheral labyrinth lesion, the fall will be in the direction of the slow component of the existing spontaneous nystagmus, no matter which way the head is turned. If the lesion producing the positive Romberg is central, it may still be vestibular in origin and then the fall will be in the direction of the quick component. If the lesion is cerebellar, the fall will be always backward or forward if the vermis is affected and always to the same side if one of the hemispheres is affected, and this fall bears no relation to the position of the head or any pre-existing nystagmus.

As I mentioned previously, I consider the spontaneous vestibular signs as more important than the induced reactions, but at times it is necessary to employ the induced tests. One can use either the turning chair or thermal stimulation, the caloric test. The turning chair has the disadvantage that it stimulates both labyrinths at the same time and, for this reason, I prefer the caloric test. Unless I am testing the peripheral labyrinth for total exclusion, I prefer to use the so-called minimal stimulation method. I slowly introduce 5 cubic centimeters of water at 80 degrees F. into the external canal after having tipped the head back 60 degrees. This co-called optimum position is used because the horizontal canals are thus put into a vertical position and we know that the horizontal canals stimulate thermally more easily than do the vertical canals. In anywhere from 10 to 25 seconds a nystagmus appears while the patient is looking straight forward, which nystagmus lasts from 1 to 2½ minutes. If the two ears exhibit a greater difference in the latent period than 5 seconds, or if there is more than 30 seconds difference in the duration of the induced nystagmus, we feel that the two vestibular mechanisms are not in balance. Fixation on the part of the patient should be prevented by the use of strong convex lenses. This minimal stimulation serves very well for studying the induced nystagmus, but is not strong enough to study induced pointing and falling reactions. It rarely produces nausea or vertigo except in the hysterical type of patient. It is needless to say that the caloric test cannot be used when there is a pre-existing spontaneous nystagmus in the central position of the eyes, nor is it of any value under these conditions.

The hearing of the patient should be tested by the voice, tuning forks, and audiometer. Bone conduction should be investigated in the Rinné and Schwabach tests. The audiometric test should preferably be done in a sound proof room. Qualitative hearing tests should not be made until the sensorium of the patient has cleared and preferably not until he is up and about. The audiometer has the advantage that it produces relatively uniform and relatively pure tones and that a graph can be made of the entire range of hearing, which can be compared to subsequent graphs and also, to some extent, to audiometric examinations made by another. Its disadvantage is that a diagnosis of the type of deafness cannot be made by its use alone. For this it must be supplemented by the use of tuning forks.

Loss of hearing due to head trauma can result from the effects of brain contusion alone, without any fracture of the cranial bones. It may result from a longitudinal fracture of the temporal bone, which courses along its anterior edge and projects itself into and through the tympanic cavity. It may also result from a transverse fracture of the pyramid which destroys the sensory epithelium of the cochlea and causes complete loss of cochlear function. Unless there has been an actual fracture of the labyrinth, in which case the loss of hearing is usually complete, the predominant type of deafness produced by a blow to the head is a perceptive or high tone deafness, associated with shortened bone conduction and a strongly positive Rinné reaction. Even in those cases in which there has been a fracture of the cranial bones

other than a direct fracture of the labyrinth, this type of hearing loss is due in large measure to the effects of hemorrhage into the labyrinth and not to the actual fracture itself. It has been proved in experimental animals that a blow to the head of insufficient force to fracture the skull will produce hemorrhages into the perilymph spaces of the basal coil of the cochlea and the harder the blow the further up in the cochlea will these hemorrhages extend. Some of this blood will absorb, but often it produces a perceptive type of deafness.

When a fracture courses through the middle ear, ruptures a drum, and damages the intratympanic structures in addition to producing the previously mentioned high tone loss, a combined type of deafness might be expected. However, when the ruptured drum closes and the fracture through middle ear heals, recovery of hearing in lower and middle tone ranges is often truly remarkable.

ROENTGENOGRAPHY

The roentgenographic delineation of basal skull fractures in general, with one exception, is very difficult even when the skull is photographed from every conceivable angle. The roentgenographic examination should include anteroposterior, lateral, oblique, vertex mental, and Stenver's exposures. Stereoscopic views are very useful. Even when all of these views fail to reveal a basal fracture, one is not justified in saying that it does not exist. Hemorrhage from the mouth or nose, suggillation about the eyes and the root of the nose, a slowly developing ecchymosis over the mastoid, the escape of blood or cerebrospinal fluid from the ear and the presence of hematotympanum are suggestive of basal fracture even in the absence of roentgenographic confirmation.

The presence of a large amount of enchondral bone in the otic capsule, bone which shows little or no tendency to regenerate permits of the roentgenographic delineation of a labyrinth fracture many years after its occurrence. So it may be said, in contradistinction to the usual failure to demonstrate basal skull fractures roentgenologically, that fractures through the petrous pyramid can almost always be demonstrated.

FACIAL PARALYSIS

Facial paralysis may be caused by longitudinal or transverse fractures, by nerve injury by stretching or tearing at the internal auditory meatus, or by hemorrhage into the fallopian canal. It may come on immediately or be delayed as long as a couple of weeks. It may be complete or partial. It complicates 10 to 15 per cent of all longitudinal fractures and about 50 per cent of all transverse fractures of the pyramid. Surgery is not indicated for this condition. Unless this complication has been caused by a transverse fracture of the petrous pyramid, recovery is the rule.

PROGNOSIS AND COMPLICATIONS

The immediate mortality from basal skull fractures is high, amounting to as much as 53 per cent according to various statistics. Late meningitis accounts for from 7 to 8 per cent mortality. The fractures of the otic capsule do not close by bony callus and, therefore, the late development of meningitis is encouraged when a mild otitis media ensues, even many years after the injury.

Most of the cases presenting a blood or cerebrospinal discharge from the ear recover without the development of meningitis unless the otic capsule itself has been fractured, and unless suppuration ensues.

TREATMENT

The principles in the therapy of craniocerebral injuries can be rapidly summarized. The first consideration after injury is the treatment of shock by bed rest, elevation of the foot of the bed, warmth, the use of shock cabinets, etc. The appearance of cerebral edema is discouraged by dehydration. This is accomplished by the limitation of fluid intake, by the use of magnesium sulphate, and by intravenous injections of glucose or sucrose. Morphine tends to increase cerebral edema and should not be used. Craniotomy should not be encouraged unless there is evidence of increasing cerebral edema or a lapse into unconsciousness after a lucid period, indicating hemorrhage from the middle meningeal artery.

Any manipulation of an ear discharging blood or cerebrospinal fluid should be discouraged as it may result in suppuration and subsequent meningitis. This cannot be stressed too strongly. Such an ear should be covered by sterile dressings which should not be disturbed for several days.

If a bleeding ear suppurates and there is no evidence of a capsular fracture, it may safely be treated as any other otitis media. A fracture of the otic capsule will be recognized by the total deafness produced. If a fracture occurs through a chronically discharging ear, a radical mastoid operation should be done as soon as patient is out of shock and fracture line should be exposed. If ever, after a transverse fracture of the pyramid, a middle ear suppuration should supervene, a radical mastoid operation should be done at once.

Needless to say the advent of chemotherapy has markedly brightened the prognosis of ear suppuration developing after basal skull fractures involving the temporal bone.

INTRACRANIAL INFECTIONS AND THEIR SPREAD FROM THE EAR AND THE NASAL ACCESSORY SINUSES

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IT always seemed poignantly dramatic in our student days to be told that there were seventeen pathways along which infection might travel from the temporal bone to the meninges and we trembled with fear at the thought of germs in the tympanum or mastoid that could choose so many avenues of attack. On an anatomical basis the unfortunate individual with a suppurative process in the middle ear and mastoid bone had a poor chance for his life. With the intracranial cavity the terminus of seventeen routes through the temporal bone, it appeared inevitable that the invading organism would find its way to the meninges and there establish a process that only a decade ago was a little less than 100 per cent fatal.

But as our clinical experience grew and furnished us practical information on the behavior of temporal bone infections, we discovered that our fears were unnecessarily exaggerated and largely unfounded. Experience did not confirm the supposition derived from anatomical study. Infection did not usually extend without restraint along the many avenues of approach to the brain but on the contrary frequently remained within the middle ear and mastoid for weeks and even months without evidence of spread beyond the confines of bone.

The usual course pursued by an inflammatory process in the temporal bone or within the nasal accessory sinuses that gives rise to an intracranial complication is one which causes a destruction of tissue by continuity of infection and ultimately reaches the subarachnoid space by direct extension through the dura mater. To be sure, there are common exceptions to this rule. We have all witnessed the tragedy of a meningitis following on the heels of a fulminating acute ear or sinus infection several hours or a few days after the onset of the disease. Or, we have witnessed the development of a septic thrombus in the lateral sinus and rapid invasion of the meninges from this source within 4 or 5 days after the first signs of an inflammatory process in the middle ear. Intracranial complications of this type are obviously due to a hematogenous dissemination of infection either in the form of a rapidly developing arteritis or phlebitis or the dissemination of septic emboli to the vessels of the meninges.

In discussing this precipitous variety of meningeal infection which, as has been implied, occurs less frequently than the more insidious and delayed form, particular emphasis should be given to the intracranial complications of the swimmer. From my point of view the acute fulminating sinusitis which develops after swimming is fraught with dangerous potentialities. There is an inordinate tendency in these cases for the infection to spread rapidly within 2 or 3 days to the intracranial tissues and to establish a diffuse meningitis or a brain abscess. The precise mechanism of such an invasion is the subject of ethical differences of opinion although in several of my cases that have come to autopsy, it was obviously due to a retrograde thrombosis of the veins of the mucous membrane of the frontal sinuses which communicate with the dense plexus of veins in the coverings of the brain. In the cases of acute sphenoiditis there were instances of cavernous sinus thrombosis with the characteristic signs and symptoms of this disease and subsequent involvement of the meninges or brain. The point is that sinusitis in the swimmer is a dangerous disease; when it invades the intracranial structures it is prone to do so rapidly and to produce a complication of serious proportions in an uncommonly short period of incubation.

All of which has given rise to a great deal of speculation and considerable acrimonious dispute on the therapeutic management of these cases. There exists a school that, for reasons which appear sound to its advocates, recommends immediate tapping of the frontal sinus with a drill through its floor or anterior wall in an effort to establish early drainage of the purulent collection. There is another group who for equally good reasons is unalterably opposed to this point of view. As for myself, I have long held to the dictum, avoid bone work in the presence of a green infection. Do not interfere surgically with a sinus involved in an acute inflammatory process. The rationale of this admonition would give rise to a discussion that is beyond the scope of this paper, suffice it to say that we are alarmed at the frequent occurrence of

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diffuse osteomyelitis of the skull after surgical attacks upon an acute nasal accessory sinus disease. In our series of 84 cases of osteomyelitis of the calvarium, the disease developed after bone work had been done in 52 cases of acute sinusitis or acute exacerbations of a chronic infection. The high incidence of this devastating disease under these circumstances would seem to point to some error of commission or omission on the part of the surgical procedure rather than to a matter of mere accident or coincidence. Consequently, it is axiomatic in our clinic to treat an acute sinusitis conservatively and to limit our surgical efforts to soft tissue drainage when the infection has perforated the walls of the sinus. Bone interference is resorted to only in the subacute or chronic stages of the disease. It is amazing and likewise gratifying to observe how frequently the acute sinus sufferer will recover spontaneously if he is given a narcotic for his pain, a shrinking solution for his nose and incision for the purulent collection that occasionally develops in neighboring tissues.

But there is another cogent reason for skepticism concerning the value of early sinus drainage by drilling through its walls, namely, the doubt that the operation can be instituted before the intracranial complications intervene. Reference has already been made to the rapid occurrence of meningitis in the sinusitis of the swimmer. There are instances by no means rare when the sinus disease and the meningeal infection seem to occur almost simultaneously. One follows the other at such a rate as to preclude the possibility of instituting a surgical measure in time to prevent invasion of the meninges. At the risk of evoking bitter criticism, I should like to pose the opinion that when the surgeon opens a frontal sinus in the acute sinus disease of the swimmer, he is usually too late to prevent an intracranial complication that was destined to occur from the onset; moreover, if the patient who has been subjected to surgical drainage does not develop a meningitis or brain abscess, there is still no justification for the assumption that the operation served as a preventive measure. Specifically, I do not believe that the end justifies a surgical means.

Come now to the discussion of another method of spread of infection to the intracranial structures, attention is called to extension by continuity and contiguity of tissue. In our experience this would appear to be the common form of invasion when the inflammatory process has progressed to the subacute or chronic stages. The infection remains active within the sinuses or temporal bone for weeks or even months, destroys the surrounding osseous tissues, and finally reaches the coverings of the brain. The dura, although a highly resistant connective tissue membrane, may ultimately succumb to the ravages of the disease. Its invulnerability to infection, however, is often amazing. An inflammatory process of uncommon virulence may grow on its surface for many months producing a large extradural abscess with pressure retention beneath the inner table of the skull without invasion of the intracranial cavity. Finally, however, the fibers of the dura may liquefy and open the subarachnoid space, an intracranial sinus, or the brain to the inflammatory process.

It is interesting to observe that a brain abscess derived from a nasal accessory sinusitis, a temporal bone infection, or an osteomyelitis of the calvarium that has passed beyond the acute stages is usually the result of direct extention to the cerebral cortex. An abscess stalk marks the line of invasion, within which it is clearly seen that the brain is attacked through a perivascular infiltration. The stalk is the result of a fibrous connective tissue proliferation and many new formed blood vessels. An infiltration of the perivascular spaces is much in evidence and it is by means of this pathological process that the infection is carried into the deeper parts of the brain.

Thrombosis of the cerebral vessels is occasionally observed in postmortem material but it is by no means the predominant method of spread. Infection from chronic inflammatory processes in neighboring bone does not frequently extend to the brain in this manner. A thorough search of many brain abscesses derived from such sources seems to indicate that the prevailing method of diffusion of infection is by perivascular infiltration and not through the migration of septic thrombi within the pial and cerebral veins.

It is to be remembered, however, that the point of entrance of infection into the cranial cavity may be widely removed from the primary focus within the temporal bone or nasal accessory sinuses. Anatomically it may be clearly demonstrated that the veins of the mucous membranes of these regions communicate directly with the dural vessels. It can be shown further that these veins may become involved in a septic thrombophlebitis which tends to distribute infection to remote regions of the dura. The typical pathological change is that of a septic exudate spreading over the surface of the dura beneath the intact inner table of the skull and frequently extending far beyond the original site of infection. Occasionally this exudate is found in one or more isolated patches under the calvarium and separated from the primary focus in the accessory sinuses or the mastoid bone by a

zone of healthy dura. Notwithstanding this mode of diffusion access to the intracranial cavity, when gained, is usually by direct extension from the exudate which is virtually an extradural abscess through the fibers of the membranous coverings of the brain.

TREATMENT

Turn now to the treatment of the intracranial complications of ear and sinus infections, reference must be made to the important matter of prevention. This has become doubly significant since the advent of chemotherapy, first, because of the masking effect of the sulfonamide drugs upon the lesions that give rise to intracranial infections and, second, for the reason that these specific chemical substances have greatly altered the prognosis of meningitis and brain abscess. It goes without saying that a surgical mastoiditis or an osteomyelitis of the skull secondary to nasal accessory sinus disease must be recognized and adequately eradicated if we are to give proper attention to our first lines of defense. Heretofore, this was not a difficult task. Years of practical experience acquainted the rhinologist with clinical pictures that were more or less typical of surgical lesions and clearly indicated the optimum time for intervention. But the introduction of the sulfonamide drugs has altered the situation somewhat in that we now encounter atypical and protein forms of inflammatory processes within bone which often keep us much in the dark concerning their surgical or nonsurgical character. Under the influence of chemotherapy, particularly its prolonged administration, a mastoid disease may run a bizarre and deceptive course characterized by remissions and a singular absence of the usual signs and symptoms. Its insidious development and perverse growth give rise to osteomyelitic lesions that do not conform to customary patterns and herein lies one of our difficult problems in the diagnosis of surgical mastoiditis in patients who have been treated with the sulfonamide drugs.

Masking, perhaps, is the word that expresses it best. It refers categorically in otological parlance to an infectious process in the mastoid bone that proceeds to its terminal stages with concealed identity. It is this quality of disguise or concealment that makes it a much feared lesion and a serious menace to its neighboring structures.

Turn now to the second influence of chemotherapy to which reference has already been made, it is a matter of verity that the sulfonamide drugs have greatly reduced the mortality of the intracranial complications of ear and sinus infections. Before the discovery of toxic chemical substances that have a specific effect upon bacteria, there was always some question in my mind as to the value, if any, of a mastoid or a sinus operation upon the victim of a meningitis. Because it seemed to be in accord with the best principles of surgery and to hold out the only hope for a cure, we routinely operated upon these patients in the early years of our experience. But the results were most discouraging. Death was inevitable in spite of our efforts and after many disappointments the futility of this practice was realized and operative procedures abandoned.

With the advent of chemotherapy and surprising recoveries from meningitis, there has been a revival of the orthodox method of treatment and renewed confidence in the practicability of surgical intervention. Once there appeared to be some hope for the life of the patient there came a strong resurgent interest in the time-honored principle of eradicating a focus of infection that was the cause of a complication. Cut off the source of supply of infection and chemotherapy will do the rest was the cry and this practice seems to have captured the approval of otologists everywhere today. So we now advocate the eradication of an infective process and mass drainage of the products of inflammation by the radical removal of carious and necrotic bone in conjunction with adequate doses of the sulfonamide drugs.

Reference has already been made to the predominating method of diffusion of infection to the brain by perivascular infiltration and in this connection we find a lesson, I believe, of some practical value. Where brain abscess is suspected it is rational to assume that the pathology of spread has been direct and therefore to search for the area of softened dura through which the disease has passed. Careful and meticulous removal of the exudate from the dura will frequently disclose the portal of entrance and give access to the pathway along which the infection has traveled. Gentle penetration of this region with a brain cannula often produces a drop of pus and reveals the identity of the inflammatory stalk. Thus we may enter and drain the abscess through a tract along which the infection has migrated and in so doing respect a surgical principle which in no other part of the body can be more advantageously applied.

At the risk of pointing out the obvious, your attention is called to the great value of chemotherapy in the treatment of ear and sinus complications. The literature is replete with references to this subject, but perhaps I may be permitted to throw a few suggestions into the hopper particularly as they pertain to the otologist's point of view.

It is highly probable that sulfadiazine will replace the other sulfonamide drugs in otological practice. It is a specific toxic substance for the Streptococcus viridans, Streptococcus hemolyticus, pneumococcus (all types), meningococcus, and Friedlaender's bacillus. While sulfathiazole is believed to be somewhat superior for staphylococcus infections, there is good scientific evidence that sulfadiazine also has a specific effect upon this organism. It is true that we frequently find a mixed infection in the ear and sinuses with the staphylococcus in great numbers but I am inclined to believe that this organism is usually a "hanger-on." The germ that puts in its first appearance, the one that is isolated with the inception of the disease and can usually be found in pure culture in the early stages is probably the real offender and the one upon which the attack should be made.

In addition to its specific effect upon all of the organisms listed above, including the staphylococcus, sulfadiazine is less toxic than its related agents. It is much less likely to produce a dermatitis, fever, vomiting, anemia, a peripheral neuritis, psychosis, acidosis, or a hepatitis than either sulfanilamide, sulfathiazole, or sulfapyradine. It may therefore be given with little risk in the home provided the patient is seen daily by the physician who will inquire into his state of health and make at least a cursory examination for the common clinical manifestations of a toxic reaction.

It is exceedingly important to commence chemotherapy at the earliest moment in the course of infection and to strike with heavy initial doses. An early knockout is the objective and to this end sulfadiazine is given intravenously in severe infections. The drug is absorbed rather slowly from the gastrointestinal tract and several precious hours may be lost if given by mouth. The initial dose should be 0.1 to 0.15 grams per kilogram of body weight of a 5 per cent solution in freshly distilled water (7 to 10.5 grams for 150 pound man). The preparation should not be autoclaved or boiled. For maintenance dosage by the intravenous route 0.05 grams per kilogram (5 to 7 grams for 150 pound man) is recommended and should be administered every 12 to 16 hours. If oral administration is utilized for a maintenance dose, 1.0 grams should be given every 4 hours. The blood level should be kept at 10 to 15 milligrams per cent.

Even when large doses of sulfadiazine are given intravenously a proportionately small quantity of it is found in the cerebral spinal fluid. This is in direct contrast to sulfanilamide which is rapidly taken into the spinal fluid and found there in rather high concentration. This observation has led to the supposition that sulfadiazine is less desirable than sulfanilamide in the treatment of meningitis. However, it must be borne in mind that in meningitis we are not treating the spinal fluid. We are treating the meninges and experience with sulfadiazine, although still meager, is promising enough to indicate that it will probably replace its allied preparations in the treatment of intracranial complications of otitic and sinus origin.

CONCLUSIONS

1. While the hematogenous spread of infection from the ear and sinuses to the intracranial structures does occur, particularly in the sinusitis of the swimmer, the usual method is by continuity and contiguity of tissue, when the primary lesion has reached the subacute or chronic stages.

2. A dictum to which we sedulously adhere is, avoid bone work in the presence of a green infection. It is admitted, however, that the exigencies of the disease make surgical intervention imperative in some cases. It may be necessary to sacrifice bone early in the acute process in order to find and drain a brain abscess.

3. Meningitis and brain abscess are occasionally chargeable to an intracranial yet extradural infection which spreads in the form of a confluent or patchy exudate over the surface of the dura beneath the inner table of the skull.

4. Treatment calls for the eradication of the primary focus of infection by surgical means and adequate doses of the sulfonamide drugs. Recent experience would seem to indicate that sulfadiazine gives promise of supplanting its allied preparations in the field of otolaryngology.

SURGICAL ANATOMY OF THE EYE

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UNDERSTANDING the anatomy of the eye is essential to any ophthalmic surgeon in performing the various surgical procedures on the globe. It familiarizes him with normal relationships, thereby giving confidence when corrective operations are undertaken in complicated cases. A knowledge of anatomy also includes an understanding of the variations from the normal and the effect these variations play on the functioning of the part. This aids the surgeon when he encounters anomalous relationships.

For instance, it is known that the rectus muscles are covered by fascial sheaths continuous with Tenon's capsule. The connection between the muscle fibers and the sheath is especially strong at the point where the two fuse. Because of this, the muscles retain their attachment to the capsule and do not retract extensively after tenotomy or enucleation of the globe. It is this anatomical arrangement which permits us to obtain some movement of the prosthesis after enucleation and implantation of a foreign substance within Tenon's capsule.

A rather uncommon, but troublesome, complication following enucleation with implantation is a tendency for the implant to migrate in the orbit as if extruded from Tenon's space. This complication may be accounted for on an anatomical basis. If we recall that Tenon's capsule and the conjunctiva are fused with the sclera for a distance of 1 to 2 millimeters about the limbus, and that the cornea has a diameter between 11 and 12 millimeters, we realize that about 16 millimeters of the circumference of Tenon's space has been lost in doing an enucleation and thus the insertion of a glass or metal ball the diameter of the normal eye made impossible. We are able to compute the exact size of ball which can be inserted into the reduced space of tenon following enucleation by subtracting the lost circumference from the circumference of the eyeball. In an adult we find that an implant of more than 18 millimeters will stretch Tenon's capsule and promote its expulsion. Those surgeons recommending a 20 to 21 millimeter diameter implant are forgetting the size of Tenon's space after enucleation. Upon severance of the optic nerve, a perforation of the capsule is made posteriorly through which an implant is easily forced if too large a one is inserted. These are minor, but important, features to remember in enucleations in which one not only attempts to get the highest percentage in retention of implant, but also to prevent migration of the implant.

In growing subjects, Tenon's capsule is easily separated from the overlying conjunctiva in the anterior segment of the globe, but in adults they are more or less fused. We rely upon the loose capsular and subconjunctival tissue as the bed for absorption of the aqueous in trephine operations for glaucoma. If the conjunctiva and capsule are separated from one another, as in Elliot's original description of the trephine operation, a rather dense scar tissue replaces the normal loose connective tissue resulting in a thin, localized, honeycombed cicatrix at the site of the trephine opening or in no bleb at all. The incision should be through the conjunctiva and capsule, and the relationship between the two should not be disturbed at any step in the operation. This has recently been emphasized by Benedict.

When iridencleisis for glaucoma is performed, it is important to remember that the conjunctiva and Tenon's capsule are fused to the sclera for a distance of 1 to 2 millimeters about the cornea. The fistulizing opening will be under a heavier and looser cushion with less chance of delayed infection, if no attempt is made to dissect the conjunctiva and capsule from the sclera further limbalward than this point of fusion before the keratome incision is performed, since the overlying tissues closer to the cornea are denser and thinner.

The sclera has very few blood vessels, and those present consist of branches of the anterior and posterior ciliaries. These form a network almost entirely confined to the episcleral tissues. This episcleral network is extremely attenuated except in the anterior region near the limbus. A close capillary system is formed here which can be evidenced clinically as ciliary injection in inflammatory conditions. This scarcity of blood supply in the sclera partially accounts for the slow healing of scleral wounds. Most of the reparative process advances from the subconjunctival and uveal tissues.

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This slow healing of the sclera promotes the possibility of expulsion of the glass or metal ball when it is implanted in the sclera as in Mules' operation. A variable amount of oozing from the perforating vessels, posteriorly and anteriorly, may result in the accumulation of a clot which exerts pressure upon the suture line. Tendency for expulsion of the implant is greatly lessened by using silk mattress sutures for closure of the scleral wound anteriorly, together with electrocoagulation of the perforating vessels on the inner surface of the sclera. It is essential for one to choose the size of implant which will permit an easy closure of the sclera without tension. Our experience in this type of treatment of the eyeball, when possible, has given a far better cosmetic result than simple enucleation or enucleation with implant in Tenon's capsule. We believe there is no more danger here of sympathetic ophthalmia than in any other form of treatment in this surgical condition. Not all cases, however, are suitable for a Mules' operation. It is reserved for panophthalmitis, freshly lacerated globes, hydrophthalmos, etc., and should not be used when tumor is suspected, or in chronically inflamed eyes.

The thickness of the sclera varies considerably with age and sex. It is thinner in children and in females. The sclera has a thickness of from 0.3 to 0.5 millimeter behind the insertion of the rectus tendon but grows thicker posteriorly. In recession operations, Jameson's directions for inserting the scleral needle should be followed explicitly. One should also remember that the tendons of the rectus muscles become thicker and denser as they approach the sclera. Therefore, if we cut these tendons as close as possible to the sclera, we will retain the densest portion and be assured that our sutures will not tear out after tying.

The limbus offers many anatomical features of clinical importance; in fact, too many to be considered entirely at this time. Schlemm's canal is commonly thought of as a single lumen. However, it is seldom a single elongated lumen, but more often consists of two or more lumina lying side by side or over one another in the scleral furrow. Salzmann describes it as resembling a great stream which flows along undivided for a stretch, then becomes divided into several branches, and thus differs in various sections of the eye. Therefore, Barkan's operation for glaucoma might fail if the incision did not happen to open the lumen, but instead passed between several branches of the canal.

The filtration angle in hydrophthalmos presents many congenital anomalies, no two being exactly alike. These congenital anomalies possibly account for the poor results obtained in the various operations most commonly used in other forms of glaucoma. In chronic noninflammatory glaucoma the filtration angle is often blocked by anterior root synechia; thus the iris does not herniate into the wound when the scleral button is removed, and no aqueous is lost. In this instance, in order to form a communication with the posterior chamber it is necessary to grasp the iris tissue with fine forceps and excise the iris. Undoubtedly all, who have performed many trephine operations, on rare occasions have experienced buttonholing of the conjunctival flap at the limbus. I have found Verhoeff's operation for glaucoma well adapted when this has occurred. The buttonhole incision at the limbus above can be continued on either side to make a short conjunctival flap. The epithelium is denuded from the upper pole of the cornea and a trephine opening is made at the usual position on the limbus. The conjunctival flap is drawn down over both the trephine opening and denuded portion of the cornea and, as in the Van Lindt flap, is sutured on either side of the cornea. In this, as in other instances, in which it is desirable to cover a portion of the cornea, the anatomical structure of the conjunctiva is such that it lends itself admirably.

The blood supply of the conjunctiva comes from the superior and inferior tarsal arcades of the eyelids and the anterior ciliary arteries. The superior tarsal arcade at the upper border of the tarsus and between the two portions of the levator tendon gives off perforating branches, which pass through the muscle of Mueller to reach the conjunctiva. Here branches are sent downward over the tarsus and upward as the posterior conjunctival vessels to form a superficial pericorneal plexus, after receiving anastomotic branches from the anterior conjunctival arteries. The anterior ciliary artery comes from the muscle branches of the ophthalmic. Each muscle artery gives off two anterior ciliary arteries with the exception of the external rectus which gives only one. The anterior ciliary arteries, after giving off the anterior conjunctival arteries, pass through the sclera at a point just in front of the muscle insertion to enter the base of the iris and form the major arterial circle. The anterior conjunctival vessels are deep to the conjunctiva and do not move with it. They anastomose with the posterior conjunctival vessels, pass on to form the deep pericorneal plexus in the episcleral tissue, and to send vascular loops into the corneal limbus. In cataract extractions, deep incisions into the limbus cut across many of these vascular loops and can cause troublesome bleeding. To avoid this trouble, some prefer to

perform corneal sections entirely in the cornea.

These limbal vascular anatomical findings are of considerable clinical interest. In conjunctivitis and inflammations of the superficial portions of the cornea, it is the superficial pericorneal plexus which is injected. In addition, these vessels move with the conjunctiva but do not fade when pressure is applied. The deep pericorneal plexus is hyperemic in infections of the iris, ciliary body, and deeper corneal stroma. The deep pericorneal plexus is injected in the form of a ciliary flush and it is noted that this flush disappears on pressure but the vessels do not move with the conjunctiva. In interstitial keratitis the new vessels invading the cornea come from the anterior ciliary arteries as they pass through the sclera to reach the iris and ciliary body.

The central third or optical zone of the cornea is spherical. Toward the periphery, especially on its nasal side, it becomes flattened. This explains, in part, the poor visual results obtained with optical iridectomies since it is often necessary to do them behind the flattened zone of the cornea. The optical effect in reducing vision is similar to that obtained in cornea plana.

Wandering cells, corneal corpuscles, and corneal lamellae make up the *substantia propria* of the cornea. The corneal lamellae are broad bands of fibrils which run the entire length of the cornea and nearly parallel to its surface. The bands of fibrils are in alternate layers which crisscross at approximately 90 degrees. This anatomical arrangement offers a line of cleavage in a plane parallel to the corneal surface for resection of corneal scars.

Many believe, in performing an iridectomy for glaucoma, that freeing the filtration angle is the purpose of the operation and that they are successful only in those cases in which the base of the iris has been freely excised from its attachment to the ciliary body. In order to remove a broad portion of the iris base it is necessary that the corneal section be made properly. Meller advises that a sufficiently peripheral position of the section can be obtained if the knife or keratome enters the sclera 1½ millimeters from the limbus and passes approximately parallel to the plane of the iris. This places the inner portion of the incision very close to the base of the iris and allows it to be excised entirely. When the inner portion of the incision is more centrally placed, the iris base is more likely to be left intact and only that portion of the iris central to the incision is removed. These faulty incisions and the iris base left fastened to the inner margin of the wound are often seen in eyes removed after unsuccessful glaucoma operations. It is best to pick up the base of the iris, push it away from the angle with the iridectomy forceps, and thus produce an iridodialysis when the incision is known to be faulty or if it is thought desirable to retain the sphincter action if subsequent miotic therapy should be needed. The base of the iris is then excised horizontally producing a large peripheral coloboma, but retaining sphincter action. Because some of the patients might need miotic therapy as an accessory aid in reducing the intraocular tension, I can see no advantage in producing a complete coloboma in either iridectomies or trephines.

The iris has a few interesting anatomical characteristics. One is its absence of hemorrhagic tendency after cutting, and another, its failure to heal following iridectomy. However, when there is inflammatory tissue on its surface or new formed blood vessels of inflammatory origin, we do find a tendency for bleeding and secondary proliferation following the trauma produced by surgery. The blood vessels in this inflammatory membrane are entirely different in character from those of the normal iris. Their walls are much thinner and contain much less contractile element; thereby giving them less hemostatic effect.

In the posterior uvea we find the choriocapillaris supplied by the posterior ciliary arteries. Anterior to the equator the blood comes from the recurrent branches of the long posterior ciliary arteries. The relatively few anastomoses between these two sources have been sited as the cause for circulatory failure of the intermediate zone at the equator in certain cases; that is, in producing the ring scotoma of pigmentary degeneration of the retina. However, ring scotoma in retinitis pigmentosa is at about the 20 to 30 degree meridian, which is in the zone of the posterior ciliary circulation and thus posterior to this junction. Ring scotoma at the equator is seen in luetic disease of the arteries and can thus be used as a differential point in diagnosing these two clinical conditions.

Between the sclera and the choroid is the perichoroidal space; a potential cavity across which the fine lamellae of the superficial layer of the choroid stretch to blend with the lamina fusca of the sclera. This space, which is traversed by the vessels and nerves supplying the choroid, stretches between the scleral spur and the opticoscleral foramen. The choroid is easily detached from the sclera during cataract or glaucoma surgery because of the delicate nature of lamellae stretching across it. Torn lamina heals without residual visual loss after absorption of subchoroidal edema fluid.

On the other hand, the inner surface of the choroid is very intimately related to the outer lay-

ers of the retina; indeed, the basal membrane separating the two structures is partly derived from each, and the pigment epithelium of the retina is very closely associated with this membrane. When the retina is detached, the split occurs between the neural layers of the retina and the retinal epithelium; the latter structure remaining behind and adhering to the choroid.

Salzmann finds that the suprachoroidea is at length completely lost in the meridional portion of the ciliary muscle. The majority of the lamellae enter the posterior border of the ciliary muscle, with the result that the most anterior portion of the suprachoroidal space must be entirely free of suprachoroidal lamellae. Because of the density of the lamina and the absence of the suprachoroidea beneath at least the anterior half of the width of the ciliary region, I would suggest that the scleral opening be at least 5 millimeters from the limbus in doing a cyclodialysis for glaucoma. This would connect the channel made to the anterior chamber with the looser suprachoroidal space behind the midpoint of the ciliary muscle.

The anatomy of this area of the globe has another important clinical application when we recall that the ciliary body has a width of about 5 to 6 millimeters (Salzmann) as measured on the inner surface of the sclera, or 7 to 8 millimeters as measured on the outer surface of the sclera. Let us recall also, that the corona ciliaris is about 2 millimeters broad, or when measured on the outer surface of the sclera 3 to 3.5 millimeters, and that the orbicularis ciliaris has a width of 4.5 to 5 millimeters on the outer scleral surface. The orbicularis ciliaris of the ciliary body contains a vascular layer much like that of the choroid with which it is continuous. It is not, however, so wide and there is no choriocapillaris. This is the least vascular structure or area of the eyeball outside of the cornea. Since the arterial supply to the whole anterior region of the uvea passes through the ciliary muscle, the vessels in the orbicularis ciliaris consist almost entirely of veins which run backward meridionally and parallel to each other to empty into the vena vorticosa. These anatomical considerations seem to point to the orbicularis ciliaris of the ciliary body as the most optimum site of entrance to remove intraocular metallic foreign bodies by the posterior route. There is no danger of detachment of the retina if a hinged scleral trephine button is made just anterior to the ora serrata and the underlying uvea incised meridionally with a cataract knife. This might occur if the opening were made further posteriorly. There is a minimum of hemorrhage since the least vascular zone of the posterior segment is entered. The postoperative reaction is surprisingly slight. The wound heals readily and without tendency for staphyloma. I can see no reason for fearing sympathetic ophthalmia. This approach has been used with much satisfaction in the University Clinic for over 10 years (1).

By recognizing the structure of the retina it is easy to understand that hemorrhage occurring in the nerve fiber layers are the flame shaped type of hemorrhages. More irregularly spreading or punctate hemorrhages are seen when they occur in the nuclear or plexiform layers. It must be borne in mind that the anatomical structure of even the largest branches of the central retinal artery resembles that of the arterioles in the thinness of their walls and in the absence or slight development of the muscular coat. Those designating the branches of the central artery of the retina in the first and second order, as arteries, and the finer divisions, as arterioles, are basing this view upon the marked differences in their clinical manifestations in hypertension, rather than upon differences in anatomical structure. Anatomically there is little, if any difference, in the various branches of the central retinal artery.

The functional retina extends to within 7 millimeters of the ora. Structurally, the nonfunctional retina is frequently degenerate and thus after the age of 30 it almost constantly shows a varying number of cysts which may in some cases atrophy to such a degree that vitreous is allowed to extend through it and cause retinal separation. Once the retina is separated, its full functions are never restored following reattachment. This is especially true when the macular area is detached in that central vision seldom, if ever, is restored to its former acuity. Most patients complain of metamorphopsia and marked disturbances in reading vision.

The peripheral retina to the extent of about 4 millimeters is seldom visible with the ophthalmoscope, even with a widely dilated pupil. This must be remembered in order to determine the distance of retinal tears from the ora in retinal separation. In less widely dilated pupils, of course, not even this much of the periphery is visible. Since the ora is considered to be 8 millimeters from the limbus as measured on the sclera, the anterior limits of the usual ophthalmoscopic field are approximately 12 millimeters from the limbus. It is convenient to remember that the optic nerve head is 1½ millimeters in diameter and to estimate the distance of the retinal tears from the ora in disc diameters. With these measurements available at the time of operation, the

position of the retinal tears may be projected to the scleral surface with fair accuracy.

The central retinal artery and vein enter the optic nerve 5 to 15 millimeters behind the eyeball on its lower and mesial aspect. The artery usually goes directly through the subarachnoid space to reach the center of the optic nerve, where it turns at right angles to send a recurrent branch backward; while the central retinal artery goes toward the optic disc. The vein enters the subarachnoid space and courses anteriorly a short distance through it before turning at right angles to reach the center of the optic nerve, where it in turn sends its recurrent branch, and then goes toward the optic disc as the central retinal vein. Thus, it is seen that the veins can be affected by any rise in pressure to which the fluid in the subarachnoid space is subjected, and papilledema may result, as in the case of increased intracranial pressure.

Fincham has demonstrated that the thickness of the lens capsule varies in different portions, and gradually thickens with increasing years. The thickest portion of the capsule is found to be limited to a zone running around concentrically with the equator and just central to the insertion of the zonular fibers on both the anterior and posterior surface of the lens. The fact that the zonular fibers weaken with age and the lens capsule thickens with age accounts for the greater ease of intracapsular extractions in elderly people.

As the anterior ciliary arteries and veins pass through the scleral emissaria anterior to the muscle attachments, they are sometimes accompanied by aberrant intrascleral nerve loops from the long ciliary nerves in the perichoroidal space. On occasions, because these nerve loops are so pigmented, they give the appearance of subconjunctival metallic foreign bodies, and unless the patient is well anesthetized excruciating pain is experienced upon attempting to remove them.

During external ethmoid operations it is of importance to remember the length of the optic nerve. The average length of the optic nerve is 25 millimeters between the globe and the optic foramen; while the average distance between the posterior pole of the eye and the optic foramen is 18 millimeters. This allows a possible forward displacement of the globe 7 millimeters before the nerve is put on a tension that might produce optic atrophy. In order to obtain better exposure during external ethmoid operations, I have seen a few instances in which too much traction on the globe has resulted in immediate and complete loss of vision.

SUMMARY

A few anatomical features of the eyeball have been presented in the hope of rationalizing various surgical procedures, and only with such knowledge is the surgeon capable of carrying out operative technique with the greatest finesse and with the least possible complications. A thorough understanding of the structures involved in a surgical problem will greatly influence the choice of method used, if several methods of approach are possible. No new operative methods have been presented, but a review of a few of the known anatomical features has been given in an attempt to draw attention to certain pitfalls in present surgical methods used on the eye which might be avoided through a better knowledge of anatomy.

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RETROBULBAR NEURITIS IN RELATION TO SINUS DISEASE

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NO subject in the entire field of otolaryngology has been capable of exciting such perennial interest and controversy, as the relationship of retrobulbar neuritis to sinus disease. Many such cases had been reported as relieved by opening of the nasal sinuses but close anatomical relationship was revealed in the studies of Onodi in 1908. He demonstrated how frequently the optic nerve passes along the upper and outer wall of the sphenoid and posterior ethmoid cells, covered only by a thin bone or membrane. To remove the effects of direct absorption of pus or the pressure from thickened membranes seemed merely to require resection of this posterior group of sinuses.

Hajek, Sluder, Sauer, Loeb, and others of that era reported many successful cases in which the blindness was relieved after such surgery. The recognition of multiple sclerosis as the commonest cause of retrobulbar neuritis discounted many of the early successful cases and incited further interest in the etiology of the disease.

It was recognized as a lesion of the papillomacular bundle with enlargement of the blind spot and central scotoma without visible change in the appearance of the eye grounds. Gradle ascribed this to the involvement of the central vein of Vossius, secondary to the involvement of the periosteal or dural veins adjacent to the diseased sinuses.

L. White (20) made most important studies, beginning in 1923, on the relationship of the diameter of the optic canal to the prognosis, finding that 50 per cent of patients with optic nerve involvement having 4 millimeter canal measurements were unimproved, regardless of the type of treatment. He showed that extensive pneumatization of the sphenoid next to the canal is usually associated with a smaller caliber canal and thinning of its bone. He urged the search for an elimination of all distant foci (21), becoming more and more conservative with regard to the surgical drainage of posterior sinuses.

As the preponderance of multiple sclerosis gave it first place in etiology of this type of optic neuritis, toxic effects from chemicals, alcohol, and tobacco, from diabetes, nephritis, and virus diseases became recognized as next in frequency, revising the figures of toxic absorption from the sinuses to the bottom of the list. Authentic reports revealing sinus disease clearly as the cause had been made by Oliver and Crowe in 1927, and Peter in 1928. Ellett in 1929 reported cases of prompt recovery of vision after drainage of sinuses as well as after removal of teeth. He emphasized the need of careful analysis of the case before selecting treatment. Benedict and Lillie in similar reports found the incidence of proved sinus infection so low in the study of large series of retrobulbar neuritis that they both considered its importance negligible. Campbell, after a comprehensive review of numerous authors giving discouraging opinions, conceded that there is in a small percentage of cases an actual indication for surgical drainage of the sinuses in retrobulbar neuritis. The study of Kennedy, in 1936, definitely established allergy as an important cause of retrobulbar neuritis to be considered in every case until any possible allergic factor has been removed from contact.

Early stages of visual disturbance in retrobulbar neuritis may be only vague subjective symptoms such as blurring which clears up rapidly. It is unlikely that many in this stage are examined. To proceed with diagnosis, multiple sclerosis must be ruled out by its numerous neurological signs and differentiated from syphilis by the use of both blood and spinal fluid serological tests. Any preceding acute febrile disease or chronic exposure to chemicals, nicotine, or alcohol is sought in the history. Foci such as diseased tonsils and teeth are carefully examined and elaborate study of the paranasal sinuses is made. Besides routine x-ray positions, lipiodol plates, made by puncture of maxillaries and by Proetz (16) displacements into sphenoids, are of great value; laminagrams made at 5, 6, and 7 centimeter levels in the coronal plane of the head, recently described by Cone, Dean, and Moore, aid greatly in the estimation of density in the posterior group of sinuses; in this district superimposed cells can be truly analyzed by this method only.

In 1939 a personal series of 13 cases (5) was presented before the Southern Medical Association,

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all of which showed lesions of the retina and choroid. The point of especial importance demonstrated by these cases was their prompt response to removal of adjacent foci, such as sinuses, and the distant foci, such as teeth and tonsils. A strict diagnosis of retrobulbar neuritis was not made in any one of that group. In the intervening 2 years 5 cases have been added to this series, each showing variations of extreme interest. In 1940 Carrol reported 100 cases studied by himself, in which he clearly differentiated between brain tumor and tobacco-alcohol amblyopia. He hoped fewer patients with upper bitemporal hemianopia with failing vision would be subjected to repeated operations on teeth, tonsils, and sinuses. His series of cases clearly showed that the tobacco-alcohol group usually occurred in older ages, consisted mostly of men, and always had a bilateral centrocecal scotoma, which was gradual in onset and recovery, not accompanied with pain on movement of the eyeball; and these patients gave a history of heavy use of tobacco and alcohol with lack of vitamin B in the diet. The majority of his patients with multiple sclerosis had already had sinus operations, however he believes that operative treatment should be carried out for diseased sinuses.

CASE 1. Mrs. D. M. B., aged 26 years, 1 month postpartum, had always had perfect health except for general allergy to a great many substances, which markedly increased during the fall grass season. For 1 week before the date of examination, February 4, 1941, she had pain over the right eye and right parietal region. She had had a severe cold with yellow discharge 2 months before which lasted a full month. Her vision began to fail after having the eye pain 5 days. Examination by Dr. John McGrath showed vision, right eye 22/100, and a hemorrhagic retinitis on the right side. The vision in the left eye was normal. Because of the marked allergic nose and lack of findings on x-ray study, operation was deferred until February 21, 1941, sphenoethmoidectomy was performed. The vision had been decreased to perception of light and dark only. The eye rapidly improved with normal vision and slight evidence of residual scarring at the end of 3 weeks. Almost the day on which Dr. McGrath reported that the vision was normal in the right eye, the left eye began to fail and tested 26/65, showing chorioretinitis with hemorrhage. She was admitted to hospital the same day and a sphenoethmoidectomy was done on the left side. Recovery of the left eye was somewhat more rapid with normal vision in 2 weeks and no sign of residual scarring.

CASE 2. M. L., aged 21 years, a male adult noticed impairment of vision without any preceding cold or throat infection. Examination of eyes by Dr. Phillip Luedde on February 24, 1941, showed vision, left eye 20/15, right eye 4/60, 2 weeks after onset. There was a large area of edema and exudate in the macular region of the right eye, accordingly the case was referred for study of the sinuses, which proved to be entirely negative. Because of marked chronic infection tonsils were removed on March 5, 1941. Recovery of the eye was extremely slow. Typical tuberculous lesions of the retina developed. He was given a course of injections of tuberculin and on October 10, 1941, 8 months after onset, the vision was 20/20, with correction in the right eye.

CASE 3. L. D. M., aged 32 years, a male adult, was admitted on the service of Dr. Lawrence Post in Barnes Hospital, with a history of complete failure of vision on the left eye for 3 days. He had carried a severe nasal infection for several weeks. Ophthalmoscopic examination of the left eye showed blurred nerve head margins, hyperemic with yellowish gray exudate and large retinal hemorrhages. The right eye was normal. The vision in the left eye limited only to light and dark. Nose and throat examination showed yellow pus pouring from the sphenoid group of sinuses on the left, and a large chronic infected tonsil fragment in the right fossa. Left sphenoethmoidectomy and removal of tonsil fragment was promptly done. He was discharged from the hospital at the end of 10 days with 20/80 vision in the left eye. One month later the vision was almost normal, but there was residual scarring in the retina.

CASE 4. B. H., aged 31 years, a saleslady, was examined by Dr. J. G. Calhoun for impairment of vision in the left eye which had slowly increased for 1 month. The delay was based on her anxiety and she had consulted several physicians before the diagnosis of macular angiospastic retinitis was made. Dr. Calhoun urged prompt removal of all foci of infection and adequate intake of thyroid, in view of her metabolism of minus 25. Yellow pus was seen grossly about the sphenoidal sinus and ethmoids on the left. She was referred to hospital on June 6, 1941, and sphenoethmoidectomy performed on the left side. At the same sitting tonsil fragments were removed. The vision slowly improved in the left eye, and October 1, 1941, was 20/20 with correction.

CASE 5. B. R. B., aged 61 years, a housewife, whose case is included in this series with permission of Dr. Theodore Walsh because of its dramatic interest. She was admitted on the service of Dr. B. Y. Alvis in Barnes Hospital December 21, 1939, with the history of recurrent iritis in the left eye for 9 months. She had an iridectomy on the left eye in May, 1939. On admission she had acute iritis, right eye, secondary glaucoma, right eye, cataract, left eye, colomba iris, left eye. No etiology was revealed in the general study. Sinus x-rays showed a soft tissue shadow on the floor of the right antrum, which was irrigated without positive finding. She re-entered hospital November 7, 1940, after a year of control of tension by use of atropine, having become sensitive to atropine. Eserine was then used, meanwhile she had had extensive tuberculin therapy. Fever therapy was started using Kettering hypertherm, and between this date and February 1, 1941, she had a total of 5 sessions. There was marked improvement of iridocyclitis in the right eye, but no change in the left.

On her admission March 22, 1941, she had become sensitive to eserine and elaborate effort was made to control the tension in the right eye. All studies were repeated, and Dr. Stanley Hamptom in consultation suggested review of the sinuses as source of bacterial allergy. In view of slight increase of density within the sinuses in a second x-ray study, Dr. Theodore Walsh advised exploring the maxillary sinuses. This was done on April 23, 1941, by Dr. Walsh, revealing the antra filled with thin foul secretion under pressure, the antral linings thickened and polypoid.

She was discharged May 7, 1941, vision in the right eye improved to 6/15, its tension reduced, remaining 15 to 20 and being easily controlled. Dr. Alvis reports on October 15, 1941, 4 months after operation, that the tension was normal in the right eye on reduced doses of pilocarpine, which will soon be discontinued.

At no stage in the observation of this group was a typical effect of retrobulbar lesion noted. There

TABLE I.—CASES OF RETROBULBAR NEURITIS (27) ADMITTED TO BARNES HOSPITAL FROM 1929 TO 1939

Age	Sex	Side involved	Concurrent disease	General therapy	Local therapy	Course
22	M	Both	Multiple sclerosis	Not treated		Not improved
22	F	Both			Sphenoethmoidectomy bilateral	Improved
38	M	Both	Alveolar abscesses	Not treated		Not improved
21	M	Both		Intravenous typhoid		Improved
27	M (Col.)	Both	Diabetes	Insulin		Improved
37	M	Both	Alcohol and tobacco amblyopia	Intravenous typhoid	Tonsillectomy	Improved
45	M	Both	Alcohol arteriosclerosis	Limit alcohol		Improved
60	M	Both	Nephrectomy 6 months before			Not treated
36	M	Both			Tonsillectomy	Improved
34	F	L			Sphenoethmoidectomy bilateral	Improved
48	M	Both	Prostatis chronic	Intravenous typhoid	Tonsillectomy	Improved
44	M	Both	Central nervous system syphilis	Fever therapy hypertherm		Not improved
53	F	Both	Hypothyroidism		Displacement irrigations	Improved
60	M	Both	Hysteria?			Not treated
34	M	Both			Tonsillectomy	Improved
36	M (Col.)	Both			Sphenoethmoidectomy Antrum windows	Improved
35	M	R.	Spontaneous pneumothorax		Sphenoethmoidectomy, right	Improved
61	M	Both	Cystoma of femur, right	Not treated		Not improved
21	M	Both	Brain tumor, osteoma of sphenoid	Craniotomy	Tonsillectomy	Not improved
32	F	Both	Brain tumor, cholecystitis	Cholecystectomy craniotomies (3)		Improved
58	M	Both		Intravenous typhoid	Sphenoethmoidectomy, tonsillectomy	Improved 2 yrs., craniotomy, death
30	F	L		Intravenous typhoid		Improved
34	F (Col.)	L		Intravenous typhoid	Cause not found	Improved
64	M	Both	Alcohol avitaminosis Hypertension	Vitamin B therapy		Improved
48	F	Both	Psychoneurosis		Sphenoethmoidectomy bilateral	Improved
20	F	Both	Allergy		Sphenoethmoidectomy bilateral	Improved
22	F	L	Allergy, hives		Sphenoethmoidectomy, left	Improved

is a variety of retinal lesions, all seen during an acute stage and all responding more or less promptly to surgical drainage of sinuses, and removal of tonsils. Cases 1 and 5 had definite allergy, the latter patient becoming very sensitive to drugs used in the eye. Although she had responded to fever therapy with remission of symptoms, the longest period of improvement began at once after clearing out the maxillary sinuses and she is more comfortable now than at any period of her complicated eye history. Case 1 belongs to the group classified as lactation amblyopia (Imachi and Maruoka, and Sautter) for which Sautter's treatment was salicylate sweats, high doses of vitamin B_1, and calcium preparations.

In a review of all patients with optic neuritis admitted to Barnes Hospital in the past 10 years —85 in number, not including records of outpatient dispensary of Washington University—it is noted that in 27 a diagnosis of retrobulbar neuritis was made (Table I). During the same period there were 195 cases of multiple sclerosis admitted

to Barnes Hospital in 1 of which a diagnosis of retrobulbar neuritis was made. The principal contributing factors noted in the 27 cases of retrobulbar neuritis were: remote foci in 6 cases; alcohol in 3 cases; brain tumor in 2 cases; sinus disease in 8 cases; systemic disease in 3 cases; complicating allergy in 2. Of the 27 patients with a diagnosis of retrobulbar neuritis, the condition of 8 was improved by sphenoethmoidectomy, 1 after 2 years; 6 were improved by typhoid and fever therapy; 2 made a spontaneous recovery with no treatment.

One is reviewed in detail with the permission of Doctors Cone and Votaw. It is of particular interest because there is an unproved allergy in the history, prompt recovery of the patient after surgery of diseased sinuses and a follow-up for 2½ years with no further visual disturbance.

CASE 6. W. W. R., aged 22 years, a white female, entered Barnes Hospital April 7, 1939, with failing vision of 3 weeks which had followed a left frontal headache with no preceding throat or nose obstruction. She gave a history of hives and angioneurotic edema in January, 1939, after eating shrimp, but no likely causative agent was taken before this attack. Examination by Dr. Lawrence Post showed vision 20/60 in the left eye with an eccentric scotoma. Nose and throat examination was entirely negative except for delayed emptying of lipiodol from the left sphenoid. Laminagrams had shown blurring of the left posterior sinus group. After consultation with Dr. L. W. Dean resection of the left sphenoid and ethmoid cells was done with marked improvement of vision in the left eye in 3 days. Section of tissues from the sinuses showed marked inflammatory change. The vision on May 10, 1939, in the left eye was 20/25—2.

Whatever is done for the relief of retrobulbar neuritis or for extensive acute retinal lesions, in the way of sinus surgery or removal of foci, should be promptly carried out, damage to the optic nerve being rapid and commonly followed by permanent residual atrophy. The opportunity to demonstrate improvement after surgery is limited because the cases showing indications are few in number, and the surgery is done concurrently with all forms of general therapy. When used there are various theories regarding the value of surgery of the sinuses:

1. Drainage of infectious material away from direct contact with the optic nerve.

2. Removal of a negative pressure effect within the sinuses which produce an emigration of toxins and bacteria to the tissues about the optic nerve (White, 20).

3. Decompression of the nerve by free incision of blood and lymphatic vessels when engorged tissues are removed (Proetz, 17).

4. Production of hyperemia, restoring blood supply to the nerve, anemic from swelling within the bony canal or by thrombosis of small vessels supplying them. Benedict and Lillie believe that the same thing may be accomplished by the use of stimulating chemicals within the nose. A most elaborate survey by Duggan, 1941, takes a strong stand against removal of foci except for the sake of removal as a toxic source—and not that such removal would influence an angiospastic lesion to which he thinks retrobulbar neuritis belongs; he considers it a localized tissue anoxia, a histamine effect, and "vasodilating therapy directed toward these pathological changes is both logical and effective—that nasal sinal surgery is nonspecific in mode of action—and that improvement of vision is more rapid and more marked (with vasodilator treatment) than when other types or no therapy at all is used."

CONCLUSION

Even though the question should remain open because of so many qualifying factors, surgery of any diseased sinuses seems to be indicated when the condition occurs in its rare association with retrobulbar neuritis. The presence of allergy increases the indication for surgery according to our experience. Study of the records certainly confirms the stated importance of removal of foci distant from the optic nerve, such as teeth and tonsils. The use of laminagrams is a valuable addition to the x-ray study of posterior sinus disease.

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MANAGEMENT OF OPHTHALMOLOGICAL SURGICAL COMPLICATIONS

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IN its broadest sense, surgical complications imply not only the complications of the actual surgical procedure, but also the undesirable and unlooked for reactions to surgery on remote parts of the body. These can be divided roughly into three large groups. The first group comprises conditions in which surgery is attended by grave risks; the second, cases in which the eyes themselves have given evidence of intolerance to any surgery. The third group is made up of cases in which one would naturally expect a good result but complications arise through fortuitous circumstances such as the patient falling out of bed or becoming delirious and pulling off the bandages and injuring the eye.

First let us consider that group of cases in which life expectancy is short, i.e., malignancy or advanced senility or great physical depression. Only the most necessary of operations should be done. Sometimes however even in advanced senility one obtains very favorable results. I remember operating on a patient at the clinic who was 96 years old and had a tumor of the iris. It seemed to be well localized but was growing. He came of a long-lived family, his father being 100 years of age at the time of death and his mother well along in years. He himself was in very good health considering his years. He recovered from the iridectomy and apparently there were no metastases. A year and a half later I removed the lens of the eye because the vision had deteriorated to less than 20/200. He recovered in the usual time without complications with vision of 20/40. There was very slight macular degeneration. He read large printed matter for several years. He lived to the age of 103 years.

In systemic diseases such as advanced tuberculosis great care should be taken not to do unnecessary surgery, particularly such surgery as will require the patient to lie quietly on his back for a day or two. In diabetes one does not worry as much as one used to. Our practice is to put the patient in the hospital for several days or a week before operation—sometimes longer—so that the diabetic service will be able to control the situation; we do not operate until that service tells us to go ahead. In acute infections such as diphtheria, scarlet fever, or acute colds one must be exceptionally careful. All but the most urgent surgery should be postponed. I recall a little Chinese boy who was brought in with a bad laceration of the eye. He had fallen on a milk bottle. The cornea had to be sewed up immediately although he had a fever of 101 degrees and a bronchitis that was very evident. In this case intravenous anesthesia was given, the eye was sewed up, the conjunctival flap was brought over, and the patient then put on the medical service. There were no serious complications.

Infections around the teeth and gums, to my mind, constitute contraindications for any but immediate surgery. The mouth should be cleaned up first and any pockets of pus or infected roots should be treated or the teeth removed. We are more apt to see these patients in the clinic than in private practice and therefore are apt to overlook the obvious.

Let us next take that group of cases in which we have learned to expect only grief; for instance, an acute inflammation in the sympathizing eye of a sympathetic ophthalmia.

CASE REPORT

Mr. Jones, No. C-15588, 74 years of age, was brought to me with a history that nearsightedness had begun 19 months before. A diagnosis of cataract had been made and the left eye was operated upon in December, 1935, about 6 months before I saw him. Apparently there was a postoperative prolapse of the iris. He left the hospital 5 days after the operation and the eye began to pain him very greatly. His doctor told him he had an infection and sent him to a dentist who found a good many of his teeth in bad condition. Nearly all of these were extracted during the succeeding several months but there was no improvement in his eyesight. At times there was very great pain which began to affect the right eye about 2 months before I saw him, that is, in May. This right eye had been perfectly normal before the operation according to his story and he had been advised that no operation would be necessary upon that eye.

I found his left vision was 0, the tension −3. The eye was markedly inflamed and shrunken. The cornea was milky and wrinkled and the eyeball was exquisitely tender. The right eye was not particularly inflamed; the vision counting fingers at 6 feet in dim light. The pupil was semidilated and vertically oval, about 3.5 by 4.0 millimeters. There was a gray reflex in the pupil. The anterior chamber was of fair depth. There were a few precipitates

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on the lower portion of the cornea and several pupillary synechiae. Considerable pigment was present on the anterior capsule and there was clouding of the cortex. No cycloplegic or mydriatic had been used in this eye according to the patient's statement.

After atropine was used in the right eye, 3 rather firm adhesions were found and there was a marked opacity on the posterior pole of the lens so that it interfered considerably with the view of the fundus. A faint view of one artery only was seen in the fundus.

In order to relieve him of pain the left eye was enucleated, and the routine medical treatment for sympathetic uveitis of the right eye instituted; salicylates, typhoid vaccine intravenously, local heat and cycloplegia. The iritis rather promptly subsided, but it would recur from time to time, lasting for a few days. The tension of this eye was within normal limits for some weeks but it gradually increased and neither cycloplegics nor miotics helped. He was carried along with a tension in the 30's for about 6 months, when the tension rose to 60 millimeters of mercury, at which time he was hospitalized and a paracentesis done. Following this the eye remained quiet for a month, when suddenly there developed considerable pain in the eye and I found a spontaneous rupture of the anterior capsule of the lens, just below the center. Cortex was found in the anterior chamber. The tension was considerably increased but the eye was too tender for us to use the tonometer.

In consultation with both Dr. Gradle and with Dr. Brawley it was decided to attempt an immediate removal of the lens and the capsule if possible. The lens could not be removed *in* the capsule naturally because the capsule had already ruptured. After VanLint akinesia and a retrobulbar anesthesia of the ciliary ganglion and 1 per cent cocaine subconjunctivally was used to assure complete anesthesia, I dissected a conjunctival flap down from about 4 millimeters from the limbus and placed the sutures before making a corneal section. The corneal section was then done, a complete root iridectomy was obtained, the nucleus and cortex were expressed and the chamber irrigated without complications. It was impossible to remove much of the anterior capsule.

At first dressing the pupil was found filled with an exudate and the iris was quite thick. The pupil remained fairly large but the anterior chamber did not form. Connected with the pupillary exudate was a yellowish white thick mass which lay on a portion of the iris and in the colobomatous area and there was a distinct tumefaction of the iris at 11 o'clock. He was markedly sensitive to atropine and scopolamine so duboisine was used. The tumefaction in the iris gradually subsided and the cornea seemed to become more normal. As the anterior chamber reformed it was filled with exudate so that there was no aqueous interval seen with the slit lamp beam. Two months after the operation there were minute hemorrhages present on the lens capsule and iris. Later the cornea became quite vascularized, the projection was very poor, the tension became minus and the sclera began to shrink. The vision of course was 0.

I cite this case for several reasons. In the first place, the time to begin to handle surgical complications is *before surgery is attempted.* This man's teeth did not suddenly become worse after the cataract operation was done. The teeth should have been put in order before the first cataract operation was done. One should also anticipate possible complications of a prostatic nature or a gall bladder nature or a bowel nature. My uncle was operated upon unsuccessfully in Florida for cataract because the doctor had not recognized a habitual cough that he could not control. This cough racked him at least twice an hour during his waking hours. Naturally he had a prolapse of the iris and a detachment of the retina. It is easier to manage these surgical complications before we attempt surgery rather than afterward.

Another reason I have cited this case in such length is because of the short period of hospitalization following the cataract extraction. The operation was done on December 3, and he left the hospital on December 8. It is true that cataracts used to be done in the doctor's office and the patient allowed to go home the same day, possibly 8 or 10 miles into the country in a farm wagon; but you would not wish to have yourself or your relatives so treated. One of the most careful surgeons in the United States keeps his patients flat on their backs for several days, occasionally 2 weeks, after the operation and practically never lets them leave the hospital under 2 weeks. Some years ago I was impressed by the action of a general surgeon who removed my wife's gall bladder. It was a beautiful operation, clean anatomical dissection, clean anatomical removal. I marvelled that he did not look at the wound for 10 days. He was sure of his surgery. He was sure of his technique. I wonder how many of us can keep our hands off an eye that has been operated upon for cataract for 3 or 4 or 5 days after operation.

Another reason I quoted this history was the fact that the patient's right vision was normal, so he said, and he quoted the doctor as saying that no operation would have to be done on the right eye. Seldom do we need to operate for cataract when the vision of the other eye is good. Very occasionally we will find an overripe cataract or a cataract beginning to become overripe in one eye and no opacity or only an immature cataract in the other eye, the vision in the second eye being nearly normal.

Still another reason is that the doctor apparently lost interest in the case at a most critical time merely turning him over to the dentist who was in a distant city. Also, he did not recognize over a period of 2 months, the beginning signs of sympathetic ophthalmia or he would not have rested until the exciting eye had been removed.

I cannot emphasize too strongly: First, the most important thing in the management of complications is to *avoid having them* by careful preoperative study of the case and by refusing to operate upon patients unless there is definite

indication therefor. Second, consultation is always in order. The patients may protest that they think highly of us but they know that none of us is all wise, and seldom do we find a patient who will not welcome consultation. The patient must have thorough confidence in the surgeon and the surgeon in himself.

One of the most difficult and one of the most usual complications after cataract extraction is prolapse of the iris. This problem has been met in several ways. The usual preventive measures have been peripheral or complete iridectomy and careful toilet of the wound; but occasionally one finds a small knuckle of iris appearing at the wound even when this is accomplished. We were taught in Vienna that prolapses usually occurred on the third or fourth day. Therefore it was not unusual to have the patient, after a cataract operation, get off of the table and be led, not carried, to his room. He was allowed to sit up in a chair until the second or third day, when he was put to bed for a few days. I saw many prolapses on this regimen. Canthotomy on unruly patients, on patients with prominent eyes or on those who are deaf or cannot understand the language is a very valuable procedure, as Dr. Gradle has recently shown. Also complete anesthesia and proper akinesia are of prime importance.

On our service at the Illinois Eye and Ear Infirmary we have found that since our technique has been slightly changed prolapses are very much fewer than they used to be. On our service there are two first assistants who alternate in the operating room, changing off every 3 months. One is a staunch advocate of the Verhoeff radiating limbal suture with conjunctival cowl. The other uses parallel corneoscleral sutures with conjunctival cowl. Otherwise their techniques are quite similar and include culture from the conjunctiva taken 48 hours before the operation and at the operation, akinesia and ciliary ganglion anesthesia, iridectomy (peripheral or complete), careful extraction, careful postoperative toilet and a preliminary canthotomy if the patient is uncooperative or the eyeball is rather prominent. Their desire is to produce nonleaking close approximation of the wound. Dr. Leech examines his patients after 48 hours, Dr. Nethercut and I, after 96 hours. In case pain or a suggestive fever occurs before the time for the regular dressing naturally our routine calls for immediate investigation of its cause. The first dressing is the most important as at that time careful handling will avoid prolapses that careless handling would produce. The careless removal of the dressings or raising of the upper lid with the thumb placed over the supraorbital notch has caused more than one prolapse. The thumb should be placed temporal to the supraorbital notch and the lid should be very gently raised.

But once a prolapse occurs, it should be recognized and notations of its first appearance made upon the record. I am not inclined to touch it for nearly a week unless it occurs within 48 hours as I wish the wound to be as firmly healed in the rest of its extent, as is possible. At the end of a week, depending upon its size and whether or not it is covered with conjunctiva, the treatment begins. If it is a small prolapse and covered entirely with conjunctiva, after anesthetizing with pontocaine, we touch the prolapse with a very small applicator dipped in trichloracetic acid. This treatment is repeated daily. It is important immediately before this treatment, to dry the area to be treated. The trichloracetic acid is a saturated solution. A dry cotton-tipped applicator should then be applied so that the trichloracetic acid will not touch other parts of the eye. This treatment is repeated daily for a week, then 3 times a week for 2 weeks. It is remarkable how many of these prolapses will flatten out under this treatment without further complication.

Larger prolapses and those not covered with conjunctiva have to be handled surgically. It is my opinion that as a rule we do not spend enough time planning our course of action, and certainly not enough time to get complete anesthesia when operation is decided upon. Also we are too anxious to get through with the operation, to cover up the eye, to hide our errors of technique with a bandage. One must be exceedingly delicate as the tissues are very thin and undue haste or pressure will cause disastrous loss of vitreous. The part must be thoroughly anesthetized by retrobulbar and subconjunctival injection as well as topical application so that there will be absolutely no feeling. This anesthetization is decidedly more difficult than at the time of the first operation. One must remember also that unless the eyeball is soft before it is opened, as soon as the prolapsed iris is cut, vitreous will present. Therefore in the retrobulbar injections, enough adrenalin must be used with the anesthetic to cause a tension of -1 to the fingers within 10 minutes. We wait until that softening occurs before opening the wound.

Some sort of a conjunctival flap must be prepared before the prolapse is excised. This can be a sliding flap or a simple cowl. Sutures must be placed in the corneal and/or the scleral tissues. If one bears in mind the histological relationship in a case of prolapse, he will better understand

how to handle the situation. A prolapse means that there is very little tissue between the contents of the eye and the outside world. At the edge of the prolapse the cornea and/or sclera are shelved to almost infinitesimal thinness. If the prolapse is large how can one expect to provide protection with only a conjunctival flap? It is essential to have the edges of cornea or sclera meet in such a way that they will grow together and be firm enough to withstand the postoperative intraocular tension. This may be aided by doing a cyclodialysis immediately after the prolapse is excised. Canthotomy will relieve postoperative pressure from without; this is imperative in the so-called "squeezers."

The actual excision is to my mind best preceded by a very light cautery, either chemical or thermal, of the epithelial structures that cover the prolapse and the nearby tissues, that is, for *at least* 2 millimeters beyond the prolapse. When the eyeball is thoroughly softened and after the conjunctival flap is prepared, one should carefully dissect down until the iris is reached at the root on both ends and on the scleral side of the prolapse. The iris is then grasped and an attempt made to free it very delicately from the *corneal* adhesions. This can usually be done with the fine forceps but occasionally a spatula is necessary. The prolapsed iris should be pulled out away from the adhesions to both distal and proximal edges and carefully excised so that the part remaining will retract. The corneoscleral edge is then very carefully prepared with the scissors in such a way that the drawing up of the sutures will cause an exact approximation of the two edges. Interrupted fine silk sutures threaded on small corneal needles are placed perpendicular to the wound so as to hold the edges together and make it watertight; they penetrate only the anterior layers of stroma. The sutures are then drawn up to demonstrate this and before being tied, their ends are passed through the conjunctival cowl. The sutures should be tied snugly but not so tightly as to invert or evert the edges. When they are tied we therefore have accurate approximation of an appreciable thickness of cornea and an appreciable thickness of sclera from the anterior surface of which all epithelium has been removed for at least 2 millimeters. The raw surface of the conjunctiva therefore has a chance to send down into these tissues new-formed blood vessels. Such an eye should be immediately treated with atropine and bichloride ointment and both eyes bandaged. It should not be re-examined for *at least 4 days*. Our recurrences are due to meddlesome inquisitiveness which should not be tolerated.

If we do our surgery well, we do not have to be meddlesome. If we do not do our surgery well, we should quit doing surgery. Prolapses sometimes occur in the best of hands but too many of them indicate poor surgery.

One of the most embarrassing complications which we encounter is an inability to extract the lens before loss of vitreous has taken place. This may be due to an improper corneal section. Recently one of the residents who had had some experience, inserted the cataract knife back of the iris. The anterior chamber in this case was particularly shallow and a corneal section should not have been attempted in the usual way. The knife was withdrawn and the section was completed by the attending surgeon with the aid of scissors. Fortunately the Verhoeff sutures had been previously placed and were ready to be tied before the attempted removal of the lens. When the iridectomy was done vitreous presented. The speculum was removed and the eye was closed for 5 minutes. The upper lid was raised with the suture which had previously been placed in it and a DeMarr retractor was inserted. The vitreous had replaced itself, the blood was washed out of the anterior chamber and on attempting to grasp the capsule with the forceps, again vitreous presented. To go after the lens in the usual way would have invited certain disaster. Consequently a thin probe with a very smooth knob at its end was used to break a few zonular fibers at a time. In order to do this the corneal lip had to be raised very gently. The fact that vitreous presented in the wound meant that some of the zonular fibers had already ruptured. Therefore the first to be ruptured intentionally were the lower ones, then those on each side, a few at a time, until nearly all of them were ruptured, after which the lens was easily removed with the loop. The Verhoeff sutures were pulled up and before being tied, the prolapsed vitreous was very carefully excised. (One must be cautious in this maneuver as the sutures can be cut so easily.) The sutures were then tied, and with a spatula, the iris was freed from the wound.

The removal of a lens freely floating in the vitreous presents many difficulties. Particularly is this so when it does not disappear into the vitreous until after the section has been made. This can best be handled by the use of a focussed fluorescent light, or by locating the lens with the ophthalmoscope, using a fluorescent light. Great care must be taken not to injure the retina as a hole is very often produced and detachment of the retina invariably results. It is considered better surgery to leave it alone unless it can be floated

into the anterior chamber and incarcerated there by contracting the pupil behind it.

Intraocular hemorrhage on the fourth or fifth postoperative day is usually not of great import but occasionally a small vessel will repeatedly bleed even after a simple iridectomy. Thorough study of the vitamin K and vitamin C content of the blood should be made. The patient's blood should be typed; we have found that small transfusions of blood repeated 2 or 3 times are usually followed by very satisfactory results. The opposite treatment—preoperative bleeding—is also occasionally successful, especially if the blood pressure is elevated. Undoubtedly preoperative bleeding of the patient used to be done too frequently. I remember Dr. Casey Woods' preoperative orders were frequently, "Be ready to take 100 cubic centimeters of blood just before the operation."

I recall the case of a friend of mine who had a glaucoma in its early stages. He very much wished to be relieved of the necessity of using drops and as the drops did not perfectly control the tension at all times, it was felt wise to operate. A simple iridencleisis was done, without complications. On the second night he hit the eye with his hand while asleep and this was followed by some pain. The next morning a small amount of blood was found in the anterior chamber. The bleeding continued until the chamber was nearly filled with blood and on the fourth day a small transfusion was given him before the chamber was opened to irrigate. The transfusion was repeated and he had no further complications.

This matter of postoperative bleeding that occurs spontaneously is often of grave concern and calls for the co-operation of an internist who is studying hematology. Small transfusions of 100 cubic centimeters or thereabouts repeated daily are often of great benefit. I have not found calcium therapy as beneficial as some have claimed it to be. Should the blood remain in the anterior chamber for any length of time there results a blood staining of the cornea. I make it a practice to evacuate it about the seventh day unless by that time it seems to be disappearing.

Postoperative glaucoma is a condition that we would see less often if we would study our cases thoroughly from the standpoint of unearthing a very early glaucoma. If we find an early glaucoma I believe that it is a point of wisdom to do a deep root iridectomy preliminary to a cataract extraction. The iridectomy should be complete if it is found that the pupil will not dilate well during the preliminary study. I believe that the tonometer is not used one-tenth as much as it should be in our preliminary examinations. In this paper we cannot take up what constitutes a thorough examination of the eyes but suffice it to say that we cannot make such an examination in 1 or 2 days. When we do find that there is a postoperative glaucoma, naturally there are counteracting measures which should be taken. One of the necessary procedures is to examine the iris first with the slit lamp and a very fine beam and second, with a gonioscopic contact glass. Gonioscopy is coming into its own slowly but surely. Just as one learns microscopy first with a low power instrument, so one should learn gonioscopy first with a simple loupe and a good spot light. The higher the magnification and the more knife-like the beam of light naturally the greater the detail.

As a rule a postoperative glaucoma shows up within a month or 6 weeks after the operation. Sometimes it is brought on by continued instillation of atropine. Occasionally it can be adequately controlled by the use of a miotic. Often, however, operative measures are necessary. These measures will depend upon what one sees with the gonioscope. If the iris angle is well open and there are no peripheral synechiae, goniotomy may be tried. This is a very simple operation and can be repeated many times. Often a single operation is effective. It need not necessarily be done under a contact glass but the eye must be thoroughly studied with a contact glass before it is attempted.

If a pillar of the iris is caught in the corneal wound and particularly if the anterior chamber is rather shallow, cyclodialysis seems to me to be the logical operation. This also can be repeated a number of times. We occasionally use air injections in the anterior chamber after this operation. The air should not be under great pressure but this procedure pushes the iris and vitreous away from the cornea. Occasionally a trephine is in order or an iridencleisis with or without sclerectomy.

In colored people we are more apt to have complications; therefore, our technique must be extraordinarily accurate and delicate. In colored people we find that it is better to do no unnecessary operating.

Occasionally we have so much postoperative reaction that the pupillary area is occluded or we have had loss of vitreous and the iris is drawn well up into the wound where it is incarcerated. We like the technique of making a meridional incision in the lower iris in all cases when a moderate amount of vitreous has been lost. This can be best done with the de Wecker or other very fine scissors and we do it just before the incision

is closed. It should be carried well down toward the root of the iris. When this has not been done and the pupil is obstructed by exudate or by the iris being drawn well up toward the wound, after the eye is quiet a small subconjunctival incision into the anterior chamber can be made from below and the iris root caught in a small iris forceps and drawn out so that an iridectomy can be done. The less done the less is the subsequent reaction. There should be sufficient adrenalin used before the operation so that there will be little or no bleeding into the anterior chamber.

Delirium is one of the bugbears we must all deal with. Recently a graduate of Rush Medical College, class of 1894, our history No. D-4107, a man of astonishing vitality, asked us to remove one of his cataracts. When he became delirious we removed the patch from the eye not operated upon, got him out of bed, and had his wife stay in the room with him; but all to no avail. Then I found he had been getting a barbiturate. The resident had just come on service and did not know that barbiturates occasionally cause a psychosis, particularly in elderly people. When paraldehyde by rectum was substituted he slept like a child and awoke refreshed and in his right mind.

We believe it important also to push fluids in elderly people; chipped ice, ginger ale, and often soda in small doses reduce the tendency to nausea and the tendency to dehydration. Infection is more easily prevented than combatted. We always take a culture 48 hours before any intraocular surgery. Small colonies of streptococci are occasionally overlooked on a 24 hour culture plate. We lost an eye some years ago because of this and since then insist on a 48 hour culture. One or two colonies of nonhemolytic staphylococcus do not cause us concern if the eyelids look normal and if we use 1 per cent silver nitrate just before the surgical procedures are begun. It precipitates the protein in the conjunctival sac if left in the eye for 30 seconds; it can then be washed out. It tends to cloud the cornea temporarily.

We always test the patency of the lacrimal passages during our preliminary survey. Appropriate measures are taken when necessary. Should the patient have a fever or should the eye be uncomfortable during the first 48 postoperative hours we do not hesitate to remove the bandage. We first examine the dressing and secretion at the lid borders. If this examination suggests infection or if the upper lid is not normally wrinkled we carefully inspect the eye. Smears and cultures are made. Atropine and a mild antiseptic such as 1 per dent aqueous mercurochrome and bichloride ointment are used, the eyes are rebandaged and milk injections are given. With the advances in chemotherapy our methods will undergo revision, I am sure. We have given one patient sulfathiazol; another had massive doses of x-ray; the former recovered; the latter did not.

I realize that many situations can arise that are not covered by these scattered remarks. The main idea that I would wish to leave with you is that surgery should be preceded by most careful study of the patient and when surgery is attempted one should bear in mind that the eye is a most delicate structure and reacts badly to carelessness.

INFLAMMATION OF THE SALIVARY GLANDS

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AT the risk of being accused of reverting to old-fashioned nomenclature the term inflammation, rather than infection, is used in the title of this paper for the reason that some of the inflammatory conditions are caused by drugs and are not primarily caused by micro-organisms. The chief purpose of the paper is to discuss the various types of infection of the salivary glands. Until I began to realize that infection of the salivary glands ties up with, and is really a part of, infection of the cervical fascia my conception of infection of these glands was indeed vague.

The process may be primary and limited to the salivary glands, or the glands may become involved secondarily in the course of a systemic disease. In the latter instance the involvement constitutes a complication, and if it occurs during an attack of typhoid fever it is none the less a case of typhoid fever and the record is filed under that heading; likewise it is none the less a case of parotitis. This makes literary investigation difficult and the witticism "always a bridesmaid, never a bride" applies.

It should be remembered that there is a close anatomical relationship of the salivary gland and lymph nodes. In the case of the parotid gland some lymph nodes are situated on the capsule and some are enmeshed in the gland itself. In the case of the submaxillary gland the lymph nodes lie on the capsule. This relationship suggests that it is possible that there may be inflammatory swelling at the location of the salivary gland which may at first be wholly a lymphadenitis. I have observed inflammatory swelling over the site of these glands, parotid and submaxillary, from infection in the lymph nodes without marked involvement of the salivary gland proper. Infection may involve the gland secondarily.

Some inflammations of the salivary glands, particularly the parotid, are metastatic. Osler designated these complicating and metastatic inflammations, symptomatic parotitis or parotid bubo. They are usually acute.

There are several specific types of salivary gland inflammation, chiefly mumps, uveoparotid fever and Mikulicz's disease or syndrome.

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MUMPS—EPIDEMIC PAROTITIS

A full discussion of this disease is not considered necessary, but a few remarks are in order. In the first place mumps is a virus disease and is definitely epidemic. All the salivary glands may be involved or only those of one side, either simultaneously or in succession. Only one gland may be involved. It is usually acute but occasionally becomes chronic due to hypertrophy. There is no suppuration. In the diagnosis it is important to ascertain the existence of any cases of mumps which the patient may have contacted within 3 weeks. An inquiry at the health department will obtain information as to the existence of known cases of mumps. It should be remembered that mumps often develops in patients after hospitalization for other reasons. In our records there are a number of instances of the development of mumps during the convalescence from injuries and operation. Obviously the contact occurred before the patients were admitted to the hospital. When the patient is in the hospital for a longer period of time the contact may be made by visitors.

It is difficult to find the records as it would necessitate perusal of thousands of histories. I was able to find the following. One case developed the day after tonsil and adenoid operation, and I am quite certain there were more; one case developed after fracture of the femur; one case after knee injury; and one 11 days after an acute upper respiratory infection. Two other cases, sisters, who were admitted to be treated for an upper respiratory infection with swollen cervical glands, developed typical signs of mumps on the day after admission.

A complicating orchitis is fairly frequent. Sometimes the lacrimal glands are involved Rarely symptoms referable to the pancreas appear. During the convalescence of one of my deep neck infection cases, a young man at home after healing was complete, swelling of the region of the parotid gland on the same side occurred with elevation of temperature. At first it was thought that a recurrence of the deep neck infection was in progress, but in 48 hours an orchitis appeared, followed in a day or two by epigastric pain and tenderness, nausea and vomiting which were ascribed to pancreatitis. The proved contact was by a sick room visitor while in the hospital. This and the

following case history are recited to demonstrate that the complications of mumps may be formidable and may bring about severe life-long handicaps. Every otologist recognizes the importance of mumps as a cause of deafness, usually bilateral. From involvement of the testicles there may come sterility; from involvement of the ear labyrinths there may come deafness; from involvement of the nervous system—brain, or meninges—there may come death. If death occurs it is most frequently from cerebral complications.

Nervous system involvements should be accorded all the care and respect that are due any involvement of the central nervous system. The following is an example. During the past year one patient with a cerebral complication caused by mumps was treated at the New Rochelle Hospital. An adult male about 45 years of age was admitted to the hospital 10 days after the onset of an attack of mumps and 1 day after he had been allowed out of bed. On the day of admission he was suddenly taken with severe headache and vomiting which continued during the day with increasing severity. The morning temperature was normal, climbing rapidly during the day to 103 degrees F. when admitted to the hospital. At this time there was also rigidity of the neck and inflammatory areola at Stenson's duct orifices. The spinal fluid showed 721 cells: 94 per cent lymphocytes, 6 per cent polynuclears; no organisms on smear or culture. By the third day the temperature had gradually come down to normal with subsidence of symptoms, and the patient was discharged at the end of 2 weeks. This patient was much depressed mentally and was considerably more ill than his chart indicated. The diagnosis was mumps virus meningitis. A prolonged rest of 3 months was prescribed.

UVEOPAROTID FEVER

Textbooks describe a condition called uveoparotid fever in which, as its name implies, there is a painless enlargement of both parotid glands with inflammation of the uveal tract of each eye. The etiology is unknown. The mortality is about 5 per cent. The swelling is firm and nodular, and usually subsides after some weeks or months. Also there is a low grade fever. Sometimes there is present one or more of the following: polydipsia, polyuria, polyneuritis, facial paralysis, burning sensation in the tongue, swelling of the lacrimal glands, and general adenopathy with splenomegaly. Visual defects are apt to be prominent and permanent. It occurs in the second and third decades of life. Tuberculosis has been accused of being the cause but this has not been proved. Treatment is purely symptomatic. The sulfonamide drugs might be tried. I have never seen a case of uveoparotid fever, and have based my description on what I have read in the books. My conclusion is that it is not common.

MIKULICZ'S DISEASE OR SYNDROME

Any reference to Mikulicz's disease without an expression of admiration for the masterly scientific description by Mikulicz in his original paper would be a regrettable omission. A delightful experience is in store for the physician who will take the trouble to read that paper in the original as translated in *Medical Classics*, vol. 2, October, 1937. To add to the wonder of the description, microscopic characteristics and blood count examinations were included when it was written, about 53 years ago, between 1888 and 1892.

The syndrome consists of symmetrical enlargement of the lacrimal and salivary glands and sometimes also of the accessory glands in the hard palate and tongue. Enlargement of the lacrimal glands is usually the first to appear but occasionally the enlargement of the salivary glands appears first, and sometimes only the lacrimal glands are involved. The swelling is firm, smooth, painless, not tender, and not adherent to the surrounding structures. Cecil states that sometimes there is splenomegaly and local or general lymphadenosis. Microscopic characteristics resemble lymphoma. The same source also states that in one of two cases observed there was general lymphadenosis with biopsy showing lymphosarcoma, the other patient recovering after antiluetic medication. It has occurred in diabetes. Hypothyroidism has also been observed with recovery after thyroid medication. The facial appearance is rather characteristic, almost grotesque, what with the swollen eyelids, the prominent jowls and the head thrown backward for vision. Naturally the patient is not pleased with his appearance, but he complains mostly of the interference with vision caused by the ptosed and puffed out eyelids. In no instance has a definite cause been ascertained. Surgical removal in selected cases has been successful, and so also has roentgen-ray therapy.

The following is a much abbreviated summary of Mikulicz's original paper. (1) The lacrimal glands are usually involved first, followed later by involvement of the submaxillaries and parotids; (2) the patient runs an afebrile course; (3) the lymphatics are not involved; (4) the spleen is not enlarged; (5) there is no leucocytosis nor other change in the blood count; (6) the disease is not a new-growth; (7) the parenchymal cells (secretory) are not involved; (8) the disease is charac-

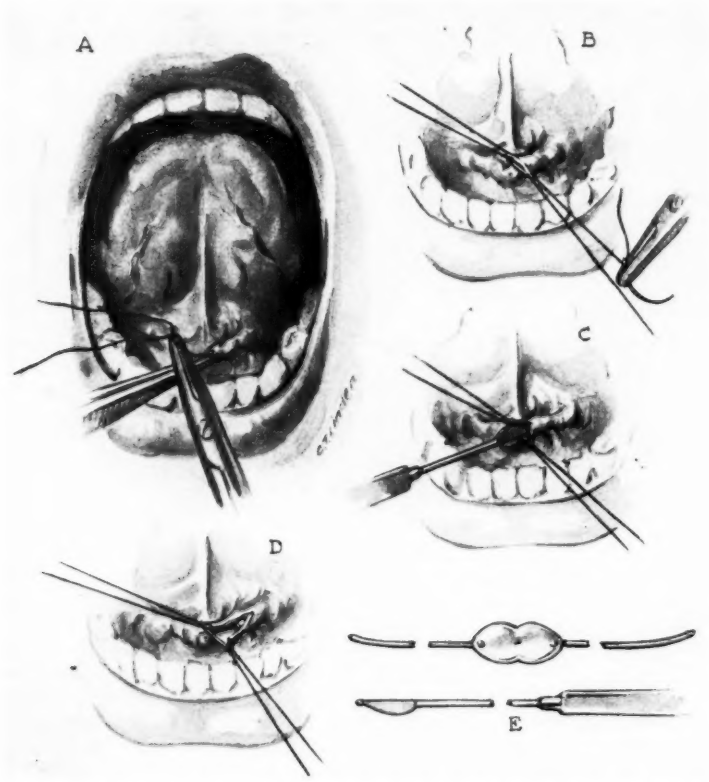

Fig. 1. A, Manner of introducing the traction sutures. B, Traction sutures in position. Note slit shape of orifice. C, Canaliculus knife in position for slitting of duct. D, Appearance after duct has been slit open, exposing calculus. E, Instrument.

terized by a round cell (lymphocytic) infiltration in the interstitial connective tissue structure, with increase in the amount of connective tissue; (9) it is essentially a chronic low grade, and not an acute, process; (10) it is not systemic—Mikulicz did not consider it hematogenous in origin; (11) he believed the causative factor to be "an infectious or parasitic process in the broadest sense of the word."

The editors of *Medical Classics* wrote the following summary:

"We know only that the disease seems to be a low grade infection of the lacrimal and salivary glands, extending over a long period with possible spontaneous termination and never causing death."

Little has been added to the subject since Mikulicz's contribution, and the problem admits of further enlightenment. Apparently all the cases which Mikulicz observed were chronic or at least nonacute, and the patients were otherwise apparently healthy.

Several years ago I observed a patient, a married woman, aged 58 years, with a low grade nonsuppurative involvement of the lacrimal and salivary glands, but with rather acute abnormalities of other systems. I regarded the lacrimal and salivary manifestations as Mikulicz's syndrome occurring in the course of an acute illness ushered in by a severe acute suppurative and ulcerative tonsillitis.

The illness extended over a period of 4 weeks during which time there were periods of sweat drenching, intermittent epigastric pain attributed to the biliary mechanism, and pain in the lower right chest region. There was throughout an extreme dryness of the mouth, or xerostomia, which symptom was not mentioned by Mikulicz as having been present in any of his cases. There was oral sepsis and caries of the teeth. Even during the early acute stage of the tonsillitis the temperature did not go over 101.4 de-

grees, the pulse running between 90 and 110. Both tonsils were riddled with multiple crypt abscesses, all probably connecting with each other and containing purulent exudate. There was also a vesicular rash, later becoming pustular, on the hands, chest, neck, scalp, and feet caused by Monilia albicans infection which yielded readily to treatment consisting of local application of gentian violet, by the dermatologist. No fungus forms were observed in the smear or the culture taken from the tonsils. Tonsil culture showed Staphylococcus aureus and Micrococcus catarrhalis. On admission to the hospital the blood indicated sepsis, with count as follows: leucocytes, 21,650; polymorphonuclears, 81 per cent of which young forms numbered 28 per cent; lymphocytes, 16.5 per cent; eosinophiles, 1.5 per cent; large mononuclears, 1.0 per cent; 1 metamyelocyte; toxic granules in an occasional polynuclear cell; no anemia. The sepsis was attributed to the severe throat infection. It gradually subsided. Roentgenographic examination of the biliary tract after intravenous injection of dye showed failure to outline or visualize a gall-bladder shadow and seemed to indicate a pathological process the identity of which was never determined. I suspect it might have been pancreatic.

On several occasions patient complained of pain in one knee joint. Blood sugar was 138 milligrams. Wassermann reaction was negative; blood culture, negative; urine sugar-free. The patient received a variety of therapy including potassium iodide, small stimulating doses of insulin, salicylates, bismuth, mixed vitamins, caroid and bile, no part of which can be said to be wholly responsible for her recovery. At first the tonsils were so swollen that they touched each other in the midline, giving rise to a type of noisy breathing with some dyspnea and at times some cyanosis. This was completely relieved by insertion of a pharyngeal airway. When the tonsillar inflammation and swelling had subsided the swelling of the lacrimal and salivary glands began to subside. She was discharged from the hospital at the end of about 4 weeks with some lacrimal and salivary swelling still present. The xerostomia was still present, but had diminished considerably. This was the driest mouth I have ever seen. It distressed the patient very much.

One month after discharge from the hospital the tonsils were removed, and since then there has been no return of the syndrome. The family doctor states that the tonsillectomy cured her. The laboratory was not requested to section and examine these tonsils, an oversight which I regret very keenly. At the time of the tonsil operation there was still present a mild xerostomia.

In the literature the ophthalmologist is the most frequently found author on the subject of Mikulicz's syndrome. This will probably continue to be the case, as the swelling of the lacrimal glands constitutes the most annoying manifestation, and ophthalmological examination is sought early. Occasionally the lacrimal glands are involved in mumps, but a diagnosis of Mikulicz's syndrome is usually justified when the lacrimal and salivary glands are simultaneously involved with nonpainful and nontender swelling. If occurring during an epidemic of mumps it should be treated as mumps. Until further enlightenment on the cause of the disease is forthcoming one cannot be more definite. Because of its microscopic resemblance to lymphoma and lymphosarcoma it has been characterized as a new-growth.

Fig. 2. Roentgenogram of typical small calculus in Wharton's duct on intraoral film.

The evidence is otherwise against it. A point of differentiation from mumps is that with mumps there is leucocytosis with lymphocytosis. Another point is that in the absence of other conditions Mikulicz's syndrome is afebrile. Simultaneous acute inflammatory involvements elsewhere, as for example tonsillitis, would be expected to alter the blood count. For the present it may be stated that simultaneous swelling of the lacrimal and salivary glands without acute inflammation, fever, or pain, and with no related general pathology may be regarded as Mikulicz's syndrome.

INFLAMMATION OF THE SALIVARY GLANDS CAUSED BY DRUGS

Inflammation of the salivary glands caused by drugs may be acute or chronic. The parotid is most frequently involved. Involvement of the salivary glands is manifested by swelling, discomfort, and alteration of function. References to this condition in the books are found under the captions, ptyalism, salivation, sialosis, sialorrhea—synonyms for increased quantity of secretion; and xerostomia, aptyalism, oligosialia—synonyms for decreased quantity of secretion. In these cases the intensity of symptoms in the mouth from the stomatitis overshadows the symptoms in the glands. Mercurialism is the best example. As an entity it rarely needs consideration. The treatment is symptomatic and abstinence from the drug. Among the drugs that cause an increased output of saliva are mercury, gold, copper, iodine, jaborandi, muscarine, tobacco, bromides, arsenic, potassium chlorate, pilocarpine, bismuth, and lead. Among those that decrease the secretion are opiates and belladonna. Personally I have had no experience with drug poisoning. Years ago I

Fig. 3. Roentgenogram showing two small calculi in the parotid gland. Cyst shown in Figure 4 was not visible in this exposure.

Fig. 4. Roentgenogram showing large cyst in right parotid gland. About 2 cubic centimeters of radiopaque solution was injected into Stenson's duct. Later, 5 cubic centimeters of cystic fluid was aspirated, from the buccal side. Photograph slightly retouched. The cyst was excised from the mouth side.

frequently saw cases of accidental and intentional mercurial salivation, the one from continuing the use of calomel for too long periods and the other in attaining the full effect of mercury in the treatment of syphilis. Calomel was then a household remedy and many cases of salivation and stomatitis resulted from its indiscriminate use by the layman.

ACUTE INFECTION OF THE SALIVARY GLANDS

The specific types of infection, notably mumps, are not here alluded to. There are three important types of acute infection of the salivary glands: (1) acute inflammation in deep neck infections; (2) acute exacerbation of the chronic inflammation wherein calculus formation occurs; (3) acute infection occurring during the course of a systemic disease or after injury to or surgical operation on abdominal or pelvic viscera. This includes severe acute pathology in the abdomen or pelvis.

There is a rare type of acute primary suppurative inflammation, usually involving the parotid gland. It occurs in infants and young children and even in the newborn. I have never observed a case. Bock and Pacella and others have reported it in the newborn.

ACUTE INFECTION ACCOMPANYING NECK AND DENTAL INFECTIONS

In my experience, acute infection in the presence of neck and dental infections is the most common type of acute infection of the salivary glands. Its place in the picture is decidedly subordinate to the deeper cervical infection. The parotid and the submaxillary glands lie in their own compartments of the cervical fascia and are separated from each other by a union of the enveloping fascia between the glands. The external layer of the parotid fascia is very tightly fastened to the overlying superficial fascia, and it is difficult to dissect the two apart. It is attached above to the zygoma for which reason swelling which involves only the parotid gland or its fascia is limited above to the zygoma. The internal surface is in relation with the sheath of the vessels. particularly the external carotid and some of its branches. The parotid gland also is in relation with small veins which enter into the formation of the common facial and external jugular veins, and less intimately with the internal jugular vein. There are a number of lymph nodes both on its capsule and enmeshed in its structure. Because of this contiguous vascularity and the rich distribution of lymphatics early sepsis is to be expected when it is severely involved. When infection of the parotid and submaxillary glands accompanies deep cervical fascia infection this may not be appreciated because of the already existing severe

sepsis. The retromandibular process or extension of the gland forms part of the external wall of the pharyngomaxillary fossa and at its end is devoid of fascia. The pharyngomaxillary fossa is divided into two unequal parts or compartments by the structures attached to the styloid process. That part situated in front of these is the anterior compartment, and that behind is the posterior compartment. The great vessels and their sheath are situated in the posterior compartment. Infection in the pharyngomaxillary fossa quickly involves the parotid gland and when this occurs the infection is both within and without the capsule. Infection in the anterior compartment of the pharyngomaxillary fossa gives an unmistakable triad of signs, viz., swelling of that lateral pharyngeal wall with protrusion inward of the tonsil fossa and tonsil, trismus, and swelling of the parotid gland. If, during the course of a deep parapharyngeal infection, swelling of the parotid gland region occurs with these other signs one may be sure of infection in the pharyngomaxillary space. The inflammatory swelling of the parotid gland increases the trismus and intensifies the pain on chewing because of its relationship with the neck and ramus of the jaw. Otalgia is not an uncommon symptom, and for the same reason. In primary inflammation, like mumps, limited strictly to the parotid gland I have never observed swelling of the lateral pharyngeal wall. Swelling of contacting or neighboring lymph nodes is present and if those in the upper adjacent cervical regions are involved the parotid swelling is continuous with the cervical swelling lower down. Tenderness is present over the whole area of swelling. It frequently happens that abscess in and about the parotid gland ruptures into the external auditory canal. I have seen this twice in deep neck infections and once when the parotid gland abscess occurred during severe inflammatory disease of the colon. Simpson has reported the occurrence in pharyngomaxillary infection. Sometimes a suppurative otitis media is the cause of suppurative parotitis.

The treatment consists of drainage of the pharyngomaxillary abscess. This is followed by subsidence of the parotid and cervical swelling, though occasionally a cervical gland abscess will form and require drainage. I have not observed a facial nerve paralysis in these acute infections, though it is appreciated that such an event is possible. I have seen and drained primary abscess of the parotid gland which I strongly suspected to have been entirely lymph node in origin. Such infections are strictly localized. The submaxillary salivary glands are more commonly involved with lymph node abscesses than are the parotid glands. In relation with the capsule of the submaxillary gland there are several lymph nodes which receive drainage from the tongue, floor of the mouth, teeth, and alveolar process of the mandible. When these nodes are inflamed and swollen the appearance is the same as when the salivary gland is inflamed and swollen, in fact some inflammation of the salivary gland itself is unavoidable. In practically all cases of the Ludwig's angina type the submaxillary salivary glands are involved, and sometimes during the convalescence after incision and drainage the glands are literally lying in a pool of pus. Infection in the submaxillary region from whatever cause practically always involves the submaxillary salivary glands, one or both. This gland is much more loosely held in its recess than the parotid gland, and as its posterior end is bent around the posterior border of the mylohyoid muscle, part of the gland is located in the mouth floor above the muscle. It is to be seen that the gland may thus be a direct avenue of infection from mouth to neck. From this it is also seen that it is a direct avenue of approach in the search for pus. Excision of the gland is practiced as a drainage measure especially, as will be mentioned later, when there are calculi in the gland. Occasionally one sees an acute infection of the sublingual salivary gland, but it is not so common. It occurs with or without calculus formation. The cause is not always ascertainable. It may be secondary to dental infection. I recently treated a patient with abscess of the sublingual gland, and no calculus nor dental pathology could be demonstrated by roentgenograms or otherwise. Cyst formation, or ranula, occurs in the sublingual glands or ducts, and is probably caused by low grade chronic inflammation. In Ludwig's angina with the pronounced inflammation in the floor of the mouth these glands are always involved, but this involvement is completely overshadowed. Acute and chronic inflammation of the salivary glands may be caused by disease of the dental region. I have seen chronic inflammation of the parotid gland, with swelling persisting for several years, accompanying dental disease for which a third mandibular molar had been extracted. There occurred osteomyelitis of the alveolar process and on several occasions acute exacerbation of the chronic inflammation in the gland. Figures 3 and 4 show a small calculus in the posterior part of the gland and a large cyst in the anterior part on the buccal aspect. The latter shows the large cyst and the duct outlined by injected radiopaque material.

I have been somewhat impressed by observance of the frequency with which dental extraction has

been the forerunner or instigator of infection in the salivary apparatus. Two cases, one in the parotid and one in the submaxillary gland, come to mind. They differ in no essential way from those not so provoked and are subject to the same indications so far as treatment is concerned. It is also possible that a latent dental infection, when interfered with or lighted up by dental extraction, may be the cause of the acute exacerbation. The relationship should be borne in mind. In the differential diagnostic relationship, diagnostic roentgenograms of both the ducts and glands and films of the jaw to exclude beginning osteomyelitis should be made.

ACUTE SECONDARY PAROTITIS

Osler called acute secondary parotitis symptomatic parotitis or parotid bubo. It is never primary and is always a complicating parotitis. It occurs during the severe febrile diseases such as typhoid, typhus, pneumonia, and septicemia. Now that typhoid fever is a comparatively rare disease in this part of the world, it occurs most frequently after severe debilitating abdominal or pelvic disease or injury. Osler stated that it sometimes occurs after injury, disease, or temporary derangement of the genital organs, and that by temporary derangement is meant slight injuries or natural processes—a slight blow on the testis, introduction of a pessary, menstruation, or pregnancy. In such cases the exact mode of involvement is obscure. In fact, knowledge of the exact pathway of involvement from the primary pelvic or abdominal disease to the gland is not yet established. Two pathways come under consideration —the blood stream and the duct system of the gland. That the blood stream is not always the pathway is indicated by the fact that the kind of infecting organisms recovered from the abscess in the gland is not always the same as the kind of organisms found in the provocative source, as for example, pneumonia. Payne has made the following observation: "There is nothing in the available evidence to suggest that pneumococcal parotitis is specially prone to arise in patients with proved pneumococcal infections. When acute parotitis develops during the course of pneumococcal infection of the lung, it is almost invariably caused by the Staphylococcus aureus and not by the pneumococcus." If the infection originates in the mouth, and it is quite likely that it does in most cases, the explanation becomes simple, but even in that event something must happen to the gland which greatly lowers its resistance and renders it more susceptible to any infection which may be present in the mouth. It is well known that in severe debilitating illness of any kind the mouth becomes septic even when it was not septic before the illness.

BACTERIOLOGY

Members of the pyogenic group of organisms are the most frequent invaders. The staphylococcus group is found most commonly, especially the Staphylococcus aureus. The streptococcus group is the next in order of frequency; also the pneumococcus. This is to be expected as this pyogenic group is most commonly present in the mouth. The typhoid bacillus would be more commonly found if typhoid fever were now more prevalent. By way of digression I should like, while on the subject of bacteriology, to refer to the types of organisms which are found in primary infections. In addition to the pyogenic group there are sometimes found fungi of which the ray fungus of actinomycosis is of particular importance in agricultural districts. In my experience here in the East actinomycosis in the mouth is very rare, but it is possible that I have overlooked some cases. The tubercle bacillus and the spirillum of syphilis are occasional invaders. Because of their frequent presence in the mouth the fusi-spirochete organisms of Vincent's angina are possible invaders, though I have never actually demonstrated them in salivary infection.

That there is an element of selectivity in the occurrence of parotitis from the numerous types of abdominal and pelvic disease is suggested by the fact that it seems to be more common after surgery of the colon. Crile and Manning, in one of the best papers on this subject, reported that over half of the cases of complicating parotitis occurred after colon surgery. The incidence of parotitis in general surgery at the Cleveland Clinic was 1 in 1,500 cases. In colon surgery the incidence was 1 in 125 cases. After abdominoperineal resections of the rectum the incidence was 1 in 20 cases. They also make the statement with regard to etiology that "modern opinion favors the ductogenous theory."

Vitamin A deficiency has been shown to cause atrophy of the epithelial lining cells of many of the epithelial structures, including the salivary glands, genitourinary tract, respiratory tract, and cornea of the eye. Following the atrophy there is metaplasia from the normal stratified columnar cells into keratinized cells which desquamate and accumulate in the ducts and acini forming masses which cause obstruction. A diminished secretion and excretion of saliva results and there is dryness of the mouth. In the presence of bacteria which are present in the duct this is the start of infec-

tion. Crile and Manning suggest that these changes, described by Bessey and Wolbach, may account to some extent for the infection in the gland.

A single parotid gland is usually involved. The reasons given for the fact that the submaxillary glands are not involved are that the normal and constant motility of the tongue and floor of the mouth tends to keep the duct clear of accumulations, and also because the secretion from the submaxillaries contains mucin, a substance which has bactericidal action. The occurrence of a complicating symptomatic parotitis is always of serious significance and immediately calls for a guarded prognosis. It occurs not infrequently in the wards of a general hospital. Cecil states that the mortality is from 30 to 50 per cent. Crile and Manning had a mortality of 43 per cent in 23 cases requiring surgical drainage. In 37 patients not operated upon the mortality was 11 per cent. In 3 cases death was attributed directly to the parotitis; in 2 cases the parotitis was contributory; in the 10 remaining cases it had very little to do with the death.

The onset is sudden with increased elevation of temperature and toxemia. There is local swelling, tenderness, and pain; sometimes painful swallowing and otalgia. Crile and Manning state that "pain in the temperomandibular joint on opening the mouth is commonly the initial symptom, occurring as early as 6 or 8 hours before swelling of the gland." If not aborted at this stage there occurs redness of the skin and fluctuation from abscess formation. In 1 of my cases this redness took on a rustiness of color almost like iron rust. I have wondered whether this is to be explained on the basis of its closeness to the overlying skin just below and in front of the lobe of the ear. In another place I have referred to the difficulty of dissecting the fascia of the gland away from the overlying superficial fascia, the 2 being quite adherent. In some cases suppurative localization takes place very slowly. In others abscess formation is rapid. When abscess has formed, large incisions are not necessary provided they go through the capsule. Incision should be withheld until one is certain that there is suppuration. Spontaneous rupture through the overlying skin and occasionally into the canal of the ear occurs if incision is delayed too long. Crile and Manning state that if roentgen therapy is applied as soon as any symptoms are recognizable the prognosis is much better in that many will not go on to suppuration. They consider the x-ray treatment very important in the earliest stage, day or night. Later its efficacy is much diminished or nullified.

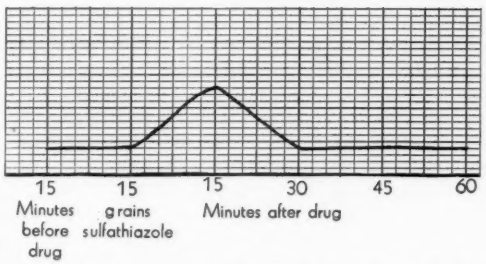

Fig. 5. Chart showing sulfathiazol concentration in the saliva with a blood concentration of 5 to 8 milligrams per cent. Note that the greatest amount appears 15 minutes after the dose was given.

Radium has also been advocated. Preoperative and postoperative oral hygiene is of the greatest importance. Cleansing of the mouth and teeth by muscular action and stimulation of the free flow of saliva, by the use of chewing gum is also of considerable value. Administration of vitamins, especially vitamin A, is also recommended because of its influence on the metabolism of epithelium. Otherwise the treatment of the parotid gland condition consists of the same measures, surgical or nonsurgical, used for any localized suppuration, but tremendously influenced by factors imposed by the primary condition. It is very advisable to begin the administration of a sulfonamide preparation 48 hours before the performance of the abdominal or pelvic operation, especially one on the colon, and to continue the administration at least that long after the operation. Since the advent of the sulfonamide derivatives, many of these dire clinical conditions should be much ameliorated, if not actually controlled, by chemotherapy.

I was able to find records of 5 cases of symptomatic parotitis in our hospital files. Our filing records do not include complications, which makes it necessary to rely somewhat upon recollection. The antecedent conditions were as follows: (1) gastric ulcer, died; (2) cesarean section with subsequent infection, died; (3) acute hemorrhagic nephritis, recovered; (4) colitis with ileostomy—parotid abscess ruptured spontaneously and healed, patient still living but very ill; (5) salpingo-oophorectomy, bilateral, also subtotal hysterectomy and appendectomy, recovered. Two of the five died.

In summing up one may reasonably state that the development of symptomatic parotitis is often contributory to the death of the patient, and always renders the prognosis of the source disease graver.

CHRONIC INFLAMMATION OF THE SALIVARY GLANDS

In the majority of instances nonspecific chronic inflammation occurs with calculus formation, and acute exacerbations take place frequently. Except during such exacerbations it causes no trouble except swelling and slight discomfort. Specific types of chronic inflammation may be caused by mumps, tuberculosis, syphilis, actinomycosis and chemicals. These also cause acute inflammations. One or more of the glands may be involved. A type of gaseous tumor formation sometimes occurs in glass blowers and wind instrument musicians. These gaseous tumors may contain purulent material.

That type of chronic inflammation occurring with calculi, either in the glands or in the ducts, is the most common. It is possible that calculus formation may be the primary condition as, for example, the formation of a solid concretion around a foreign body such as a seed, piece of tooth-pick, piece of fish bone, etc. In such cases chronic inflammation of the duct and gland is inevitable and sooner or later, as the concretion increases in size, more or less constant or intermittent obstruction to the outflow of secretion results. The signs of obstruction are intensified during meal time when an increased amount of secretion is called forth. The signs are increased swelling of, and discomfort in, the gland. Sometimes there also occurs sudden filling of the mouth with a gush of released secretion. There is also swelling and discomfort in the floor of the mouth. Acute inflammation may occur suddenly with marked increase in the severity of the symptoms. Sudden obstruction in the presence of duct stone does the same.

Calculi may form during the course of a chronic inflammation and as an incident in the process. In other words it may be secondary. The same type of inflammation may not be accompanied by the formation of any calculi. It may in some instances be likened to the age-old problem of the priority of the hen or the egg. Clinically it may be regarded as the same condition whether or not calculi are present. It is probable that sometimes there is actually calculus formation present when it has not been demonstrated by diagnostic roentgenogram prior to surgery.

New and Harper have published valuable statistics on this subject. They found that in only 63 per cent of 110 cases of nonspecific chronic inflammation could they demonstrate the presence of calculi. Forty-two per cent of these were removed from the duct, 18 per cent from the gland through the floor of the mouth, and in 4 per cent the gland was excised with its calculus content. They state that clinically the condition is the same whether or not a stone is present. Statistics vary somewhat as to the relative frequency of involvement of the several glands and ducts with and without calculi. New and Harper report the following percentage of incidence of salivary calculi according to the gland or duct involved. Submaxillary gland or duct, 92.9 per cent; the parotid gland or duct, 4.3 per cent; the sublingual gland or duct, 2.8 per cent. Wakeley reported as follows: submaxillary, 63.2 per cent; parotid, 20.6 per cent; sublingual, 16.2 per cent. Czygan reported 37 cases as follows: Wharton's duct, 59.4 per cent; submaxillary gland tissue, 10.8 per cent; Stenson's duct, 13.5 per cent; parotid gland tissue, 2.7 per cent; sublingual duct, 10.8 per cent; Bartholin's duct, 2.7 per cent. Blair stated that the most common location of salivary calculi is in the submaxillary (Wharton's) duct, being more frequent there than in all other locations combined. That about sums it up. It occurs in middle aged people, and according to various writers, from two to five times as frequently in men as in women. Curiously the right submaxillary gland and duct are more frequently involved than the left.

In those cases of chronic inflammation without stone, New and Harper report that the submaxillary gland was the most commonly affected. The incidence was as follows: submaxillary gland, 80 per cent; parotid gland, 12.5 per cent; sublingual gland, 7.5 per cent. Of the 40 there were 27 males and 13 females. In all of them tuberculosis, syphilis, and actinomycosis had been excluded as etiological factors. It should be possible to demonstrate nearly all salivary calculi by roentgenogram because they are composed mostly of calcium carbonate and calcium phosphate. It has been stated that the saliva of the submaxillary salivary glands has a higher percentage of solids and organic matter which should permit the calcium salts in these glands to be seen more distinctly than those in the calculi of the other glands. The factors which make tartar prone to form on the lingual surface of the lower incisors may also favor the formation of calculi in the submaxillary ducts and glands. A history of previous attacks, sometimes dating back years, is commonly elicited. The most prominent symptom or complaint is intermittent pain and swelling of the gland caused by acute exacerbations. Pus can be expressed from the duct by making pressure on the gland during acute exacerbations and nearly always when no acute inflammation is present if there are calculi in Wharton's duct. The same with regard to the parotid and its duct.

The orifice of the duct is inflamed and prominent, and in most cases a stone in Wharton's duct can be palpated with the finger. In the case of Stenson's duct this will depend on its proximity to the duct orifice. Farther back than where the duct goes through the buccinator muscle it would probably not be palpable unless very large. Roentgenography, including exposure on an intraoral film, in my opinion is very valuable. In former years before the development of the precise roentgen technique of today it was often disappointing. Sialograph after injection of radiopaque solution, 1 to 3 cubic centimeters, has in my experience helped to differentiate between a duct and a gland calculus. It should not be done during an acute exacerbation. It is particularly helpful in the parotid duct and gland cases. I see no objection to careful probing except during acute exacerbations. It may be done in both Stenson's and Wharton's ducts, and is sometimes very helpful. If the duct is traumatized by rough manipulations an acute inflammation may be precipitated. I have recently considered the feasibility of injecting 1 to 3 cubic centimeters of a sulfonamide solution into Stenson's or Wharton's duct for these inflammatory conditions in which the calculus is in the gland or in which there is no calculus in the duct. To date I have not done so.

PATHOLOGY

Sometimes a calculus is extruded by erosion and formation of fistula, usually into the mouth but occasionally through the skin. It was submaxillary in all reported cases. If it occurs externally branchial and thyroglossal fistulas must be excluded. Calculi usually occur singly but may occur in numbers. Most of them are smooth but in one of my cases it was so rough and so firmly attached to the walls of the duct that it was necessary to detach it by sharp dissection. It had a surface similar to the rough irregular surface of an inferior turbinate bone. If the obstruction is complete, cystic dilatation of the duct behind it occurs, and congestion followed by atrophy takes place in the gland structure. In the duct itself there occur congestion, petechial hemorrhages, granulations, and fibrosis.

The following is a pathological report from one of my cases of chronic inflammation of the right submaxillary gland with calculi in the gland: I quote from pathologist's report.

"Gross examination: A submaxillary gland 6 by 4 by 2 centimeters in size. It has been cut in the longitudinal plane, exposing two small calculi deep in the substance of the gland. The cut surface is pinkish yellow in color and has coarsely lobular markings. . . .

"Histologic examination: Sections show acute and chronic inflammatory changes in submaxillary gland with proliferation of small ducts and compression and distortion of the gland alveoli. Many small ducts contain purulent exudate. The uniform lobulation, the marked inflammatory changes and the presence of calculi make it appear proper to classify the growth as a salivary duct adenoma.

"Diagnosis: (1) submaxillary gland duct adenoma; (2) acute and chronic inflammation, submaxillary gland; (3) submaxillary gland calculi."

Another of our cases carries the following histological report. No calculi were present in this one.

"Sections show greatly distorted submaxillary gland, with obliteration of gland units and productive inflammatory products between atrophic gland units. There is no evidence of tumor. Diagnosis: Chronic inflammation, submaxillary gland."

Citation of more examples would be needless repetition, as these serve to show the typical pathology. Henke and Lubarsch, quoted by New and Harper described these two types of chronic inflammation of the salivary glands, designating them chronic exudative and chronic productive, respectively. Fibrosis is as good a name for the latter variety and is more descriptive. Cysts, quite large, also form occasionally. I now have under observation one such case in which the cyst was excised from the inside of the mouth. It was situated in the anterior part of the parotid gland.

TREATMENT

Treatment is in most instances surgical but should not be done during acute exacerbations. If there is acute inflammation hot fomentations externally with hot saline mouth wash are valuable. Administration of the sulfonamide derivatives, preferably sulfathiazol or sulfadiazine, is advisable, and otherwise any symptomatic treatment that may be indicated. Probing should not be done during acute exacerbations. When the acute attack has completely subsided, usually after several weeks, the calculus may be removed or the gland excised as indicated. For probing the duct (Wharton's) or removing a calculus I prefer to immobilize the duct at its orifice in the papilla with two silk retraction sutures as suggested by me in 1934 and here illustrated in Figure 1. Immobilizing the calculus against the inner side of the jaw with the finger, and cutting down upon it directly is the most commonly employed method of removal. When the calculus is small it is not always easily palpated, in which case cutting directly down upon it is sometimes difficult. When traction is made with properly placed silk sutures the orifice is converted into a long slit into which it is extremely

easy to pass the end of almost any kind of a small instrument. They also give good immobilization.

It should be remembered that the ranine artery, lingual vein, and lingual nerve are all on the tongue side of the duct, and therefore when working in this region one should work toward the jaw side as much as possible to avoid these structures. Excision of the submaxillary gland is the indicated procedure when the gland is severely involved, with or without calculus. This is comparatively simple, but one must identify vessels and nerves, most of which are in relation with its posterior and internal aspect, namely, the facial vein, the facial artery and the hypoglossal nerve; deeply also, the lingual nerve. The facial nerve should be well out of the field. If an abscess forms it should be drained, but extensive dissection for the removal of calculi should not be done until all acute inflammation has subsided.

The foregoing applies to the submaxillary gland. The problem is more complicated in the case of the parotid gland because of anatomical location and relationships. The drainage incision for parotid abscess should never be made vertically because it will cut across the branches of the facial nerve. A horizontal incision parallels the nerve branches and avoids this. Stenson's duct perforates the buccinator muscle not far from its orifice in the mouth, and beyond this point lies between the muscle and the skin of the face. Any incision of the duct within the mouth farther back than about 2 centimeters from its orifice must involve this muscle, and from the mouth aspect is deeply placed. Incision into the duct should never be made externally through the skin for fear of producing a salivary fistula, and this is to be avoided at all costs. Excision of the parotid gland is a formidable procedure and is practically never done except for malignant growths. Drainage of gland abscess should be done promptly when the indications arise. Usually small incisions that penetrate the capsule, parallel with the branches of the facial nerve, suffice. The skin incision may be a single larger one. Injury to Stenson's duct must also be avoided. I have seen salivary fistula develop from a pocket-knife stab wound in the sulcus between the tip of the mastoid process and the angle of the jaw. It was not in the vicinity of Stenson's duct nor did it involve the facial nerve. A wound in the gland does not always cause fistula. In that case it was decided to produce glandular atrophy by means of roentgen therapy but to date this has failed. At the time of the injury it was necessary to ligate the carotid.

The last case of acute symptomatic parotitis in our wards developed on the fourth postoperative day. Four days later the otolaryngologist saw the patient in consultation and immediately prescribed sulfadiazine in full dosage, attaining a concentration of 8.2 milligrams per cent. The swelling subsided in 48 hours without recurrence, and the patient convalesced from the pelvic operations uninterruptedly. This is a striking example of the effect of the new weapon we now possess in the sulfonamide derivatives. Without their help such a case might have gone on to a disastrous septic termination or at the least a stormy septic bout. From observations made over the years before these drugs were available I have been convinced that the patient is never again the same healthy individual he was previous to the infection. It may be true that he will have acquired a more or less temporary strong immunity to the particular type of infection, but at the expense of irremediable damage to such vital organs as the heart, liver, and kidneys, which in time will make itself manifest. Therefore the long range effect of these drugs in cutting short these severe infections is incalculable.

After reviewing the history I had the desire to know whether or not any of the drug is excreted in the saliva, and if present the approximate quantity. With that in mind specimens of saliva were collected at intervals after the administration of the drug by mouth. The drug was given in capsules to minimize or avoid any retention of it in the mouth. We were considerably handicapped by the shortness of time at our disposal, and the following meager results are submitted in the hope that others, better equipped than we, will make more comprehensive and conclusive investigations.

Our resident house officer, Dr. P. E. Noonan, made a survey of the house, and from each of the patients who was receiving a sulfonamide derivative, regardless of the kind of illness, collected saliva specimens of as large a quantity as the patient could produce, at the following intervals of time. The first specimen was taken 15 minutes after administration; the second, 30 minutes after; the third, 45 minutes after; and the fourth, 1 hour after. The doses were spaced 4 hours apart. As there were too few who were being started on the drug those who had been taking it for varying periods of time were included. As you know, the quantitative estimations are done by colorimetry, and in the saliva these color reactions can be seen but are too small to be measured. In other words the concentration is far less than even a low blood concentration and it is not possible to designate it in figures. It is therefore approximate in the extreme. However, it was unmistakably seen that

the deepest coloration in the saliva almost invariably appeared in the first, the 15 minute specimen, but once in the 30 minute one, probably because of a slower rate of absorption of the drug in that patient. In those cases which had been receiving the drug the saliva concentration was again at the level existing prior to the administration of the dose at the end of one hour. In those receiving first dose it had completely disappeared in one hour. Nine tests were made with no variations in results.

Two conclusions may be definitely arrived at: First, there is at no time a high concentration in the saliva, in fact it is very low. Second, the highest concentration appears in from 15 to 30 minutes after administration of the dose, and quickly diminishes. From all this it may therefore be concluded that any influence of the drug on infection in the salivary glands comes from the concentration in its circulating blood, and that any influence from that in the salivary secretion is practically negligible. How much, if any, may accumulate in the gland secretion when there is obstruction to its outflow is not known. On the other hand it may be definitely stated that there is a very small amount of the drug in the saliva while it is being taken by the patient. In other words the secretory cells of the glands do pass some of it through.

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REFINEMENTS OF GENERAL SURGICAL TECHNIQUE AS APPLIED TO OPHTHALMIC OPERATIONS

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IN a consideration of the evolution of modern ophthalmic surgery in relation to general surgical technique, it is often merely inferential to associate certain ocular surgical techniques with the practices of the general surgeon. However, most ophthalmic surgeons obtained their early training in general surgery and undoubtedly received their first inspiration from the masters of general surgical technique.

The practice of eye surgery is based upon the same 3 fundamentals governing general surgery: (1) the control of hemorrhage, (2) the proper anesthesia, and (3) the prevention of infection. Improved methods of controlling hemorrhage and better anesthesia have made the rapid, skillful eye surgeon, whose surgical judgment may not have been too good, less important than the thoughtful, careful but possibly less brilliant technician. Better methods of preventing infection have greatly lessened deformity and blindness from this source. That modern ophthalmic surgery owes a great debt to the pioneers who dared to break away from the routine, conservative, and often antiquated practices to undertake new methods and new techniques in surgery is evident. We know that Harvey, who discovered the circulation of the blood, received the ridicule of his colleagues; he and his followers were called "circulators" which meant quacks and charlatans. The men associated with the development of ether anesthesia had tragic fates with the exception of Long.

Pasteur, who destroyed the theory of spontaneous generation and laid the foundation for the prevention of operative and postoperative infection, worked for years without recognition. Unless Lister had been prepared to receive the message of Pasteur and carry on his work of preventing wound infection in spite of the active opposition of his colleagues, he would never have introduced the Listerian principle of antiseptic surgery, upon which modern ophthalmic surgery is founded.

To determine exactly where credit is due for present day ophthalmic practice is difficult, for many surgical procedures are of ancient origin. For example, ligature for the control of bleeding in wounds was used by the Greek and Roman surgeons. Therefore, one is inclined to agree with Ambroise Paré, who said "you will have to render an account not to the ancients but to God for your humanity and skill."

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ANESTHESIA

General anesthesia has been and still is of great importance in the development of ophthalmic surgery but for most operations local anesthesia is preferred. Before a general anesthetic is administered it is advisable to quiet the patient by the use of chloral and bromide by rectum or by the administration of morphine and hyoscine.

Flagg's intratracheal inhalation anesthesia is a valuable improvement in administering ether. It has facilitated the performance of delicate eye operations, as recession and cataract, as it eliminates disturbing head movements and congestion of the eyes, and lessens the danger of lung infection.

Rectal anesthesia with avertin (19, 77) is especially useful in ophthalmic surgery in preventing fear of operation in young children.

Intravenous anesthesia with evipal (sodium evipan) has been used in paracentesis, enucleation, evisceration, cataract, trephine, iridectomy for acute glaucoma, exenteration of orbital growths and squint (56). However, cases in which vomiting (15), sneezing, sobbing, and postoperative restlessness occurred have been reported. When intravenous injections can be made, this anesthetic is satisfactory for short operations (72).

Local anesthesia with cocaine, applied to eye surgery through the brilliant research of Koller, was undoubtedly even more important for ophthalmology than general anesthesia. Cocaine is still used in ophthalmic operations when vasoconstriction and dilatation of the pupil are desired. Because pantocain is less irritating than cocaine and produces less drying of the epithelium, a one per cent solution of this drug (78) is gaining popularity as a local anesthetic for eye surgery.

The development of procaine (novocain), which is much less toxic than cocaine (16), led to the more constant use of deep injections about the eye for anesthesia and akinesia. A solution of procaine and adrenalin is employed in Gradle's application

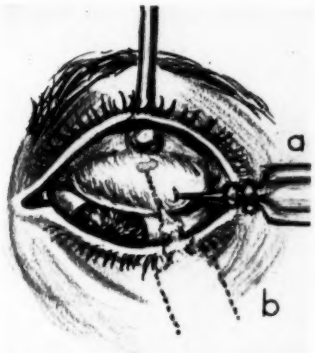


Fig. 1, left. Tarsal anesthesia (Gradle). *a*, The point of the needle is introduced through the conjunctiva at the temporal edge of the tarsus and passed parallel to the upper edge of the tarsus, thus ballooning out the retrotarsal fold. *b*, The needle is pushed slightly toward the skin side, thus thoroughly anesthetizing the entire eyelid including the skin and conjunctiva.

Fig. 2. Modification of the Van Lint method of producing akinesia.

of the method of nerve block anesthesia (31) to surgery of the eyelids (Fig. 1). In this procedure, the point of a 25 gauge hypodermic needle is introduced through the conjunctiva at the upper temporal border of the tarsus. One or 2 minims of a solution of procaine and adrenalin is injected at this site and the needle is passed forward parallel to the edge of the tarsus, thus ballooning out the retrotarsal fold.

In spite of the numerous advances in anesthesia, the ophthalmic surgeon still awaits the development of a pill or capsule which will cause rapid, prolonged anesthesia without complications.

AKINESIA

Modification of Van Lint's method of producing akinesia. Because Van Lint's splendid method of akinesia sometimes produces too great and prolonged relaxation of the eyelids, the following technique has been developed: A 26 gauge needle, 25 millimeters in length, is inserted subcutaneously 8 millimeters temporal to the external canthus. The needle is pushed forward as the plunger forces the procaine (2 per cent, 2 drams) and adrenalin (3 minims, 1:1000 solution) under the skin of the upper eyelid as shown in Figure 2. The needle is then partially withdrawn and inserted in the lower eyelid, ballooning the tissues over the outer third of the lower eyelid. A second puncture is made at the center of the eyelid, 3 millimeters above the orbital margin, and the needle directed toward the inner canthus, thus the solution balloons the skin.

In the *O'Brien method of akinesia* (49) the point of injection is just anterior to the tragus of the ear, below the posterior portion of the zygomatic process and directly over the condyloid process of the mandible. From 1 to 2 cubic centimeters of a 2 per cent solution is injected at a point directly over the exit of the branch supplying the orbicularis; while the remainder is injected superficially under the skin and spreads fanlike, in a forward direction, above and below the eyeball (Fig. 3). When a patient has an extremely broad face, complete akinesia may not be produced by the O'Brien method, even with a second or third injection. In this event, the modification of Van Lint's method of producing akinesia is indicated. However, the more remote the site of the injection from the field

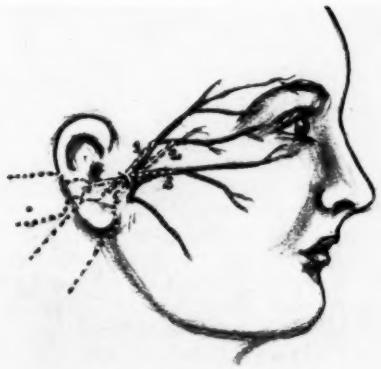


Fig. 3. O'Brien method of akinesia. Injection of the upper, *1*, middle, *2*, and lower, *3*, branches of the seventh nerve.

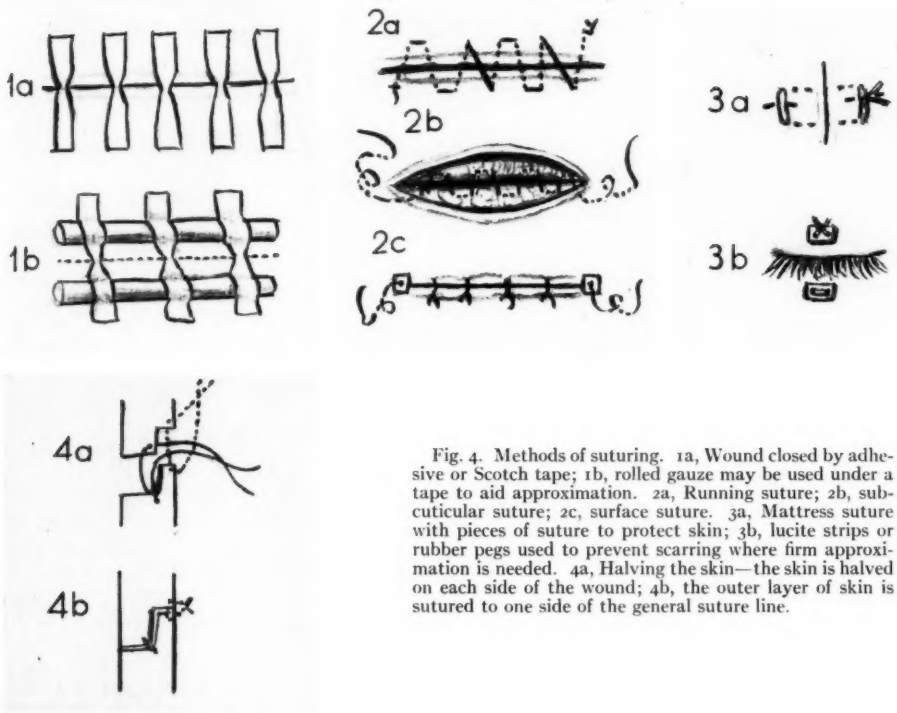


Fig. 4. Methods of suturing. 1a, Wound closed by adhesive or Scotch tape; 1b, rolled gauze may be used under a tape to aid approximation. 2a, Running suture; 2b, subcuticular suture; 2c, surface suture. 3a, Mattress suture with pieces of suture to protect skin; 3b, lucite strips or rubber pegs used to prevent scarring where firm approximation is needed. 4a, Halving the skin—the skin is halved on each side of the wound; 4b, the outer layer of skin is sutured to one side of the general suture line.

of operation, the less the danger of complication; therefore, the O'Brien akinesia is preferable to the injection of the eyelids, especially for plastic operations.

INCISIONS

Knowledge of the healing of skin incisions dates from the time of Hippocrates, who operated for calculi in the kidney by incision. Diocles Carystius (*circum* 350 B. C.) bandaged the head for wounds caused by darts. Theodoric (1250) of the order of the Preaching Friars taught that wounds should heal by first intention and that suppuration was unnecessary. As it is so well established today it seems impossible that Paracelsus had to fight for this principle as late as the sixteenth century.

Wounds were closed by adhesive strips and by rollers and compressors until animal gut sutures were employed by Rhazes (A. D. 852). Physick (1768) experimented with buckstring, French kid, and animal gut as ligatures. In 1848, W. T. Wragg wrote on the use of sutures in surgery and their advantages over adhesive strips and other modes of coaptation of the edges of wounds. Adhesive tape and Scotch tape still have their uses. Because there is little danger of death from the separation of eye wounds, the use of adhesives as advised by general surgeons (23) is valuable in primary and secondary wound closure when fear or shock is to be avoided. It is usually advisable to cut a notch in each side so that the strip will be narrow where it crosses the wound. If the tape is flamed, it will usually hold better.

Postoperative scars. Ophthalmic surgeons have learned much concerning the prevention of scarring from the teachings of general and plastic surgeons. For example: (1) The incision must be made with a sharp knife and part of a safety razor blade is advised by the plastic surgeons to insure a sharp edge. However, since cataract knives may be sharpened so well, many ophthalmic surgeons use these knives for other than cataract incision. (2) The incision should not cut across the skin lines and must not be beveled because epidermis cannot be approximated with epidermis and corium with corium if the skin is beveled. (3) Effort should be made to avoid a jagged edge. (4) If the surface sutures are the finest obtainable, include only epidermis, and are placed without tension,

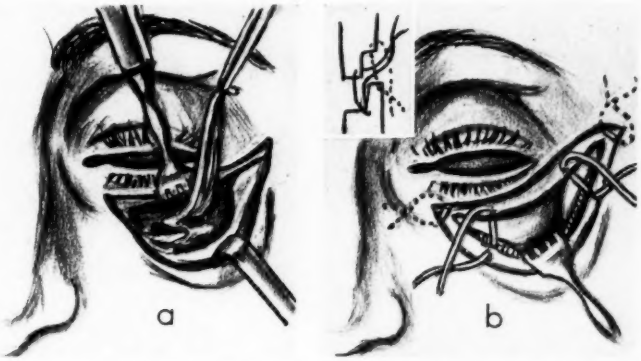


Fig. 5. The halving operation (Wheeler). a, inserting fascia lata in depressed wound in malar region; b, and insert, method of suturing skin which has been halved.

after the layers of the corium have been accurately approximated, excellent results are obtained. However, there is usually some uncertainty about suturing the different levels of the skin accurately, and halving the skin, as suggested by the general surgeons, permits accurate approximation of the epidermal layers. On one side of the incision the outer half of the skin is excised and on the other side the inner half of the skin is removed. These incisions of the skin need be only a few millimeters in width, the wound edge on which the deeper tissue has been removed is drawn over the surface of the wound edge, the outer surface of which has been removed (Fig. 4).

Wheeler used the halving operation for lower eyelid and malar bone deformities (Fig. 5).

After proper coaptation has been obtained, infection is the most serious danger to healing and each stitch should be observed daily. Keloid is particularly disfiguring and the general surgeons have pointed the way here by suggesting excision and radium treatment (61).

SUTURES AND SUTURING

Largely because of the delicacy of ophthalmic surgery, needles and suture material have been constantly improved. Most ophthalmic hospitals now have atraumatic needles available in various sizes, threaded with fine catgut and No. 000,000 to No. 00,000,000 white and black silk. Mersutures on curved eye needles, No. 000,000 black gossamer silkworm, have been useful in plastic surgery of the eye. I have found nylon sutures of value in transplanting Tenon's capsule (7) and in resection (4) and retroplacement operations (9) for strabismus; nylon sutures have also been found of value for closing skin incisions.

Much of what ophthalmologists have learned concerning the use of new suture material has been derived from their general surgical application, for example, the dangers of catgut. In the time of Lister, catgut had been tried often and as often abandoned. The factors governing the loss of strength of catgut when embedded in tissue were pointed out by Howes. He found that (1) in the presence of fluids such as physiologic sodium chloride solution or of blood serum, the tensile strength is moderately diminished; (2) in an inflammatory exudate composed in large part of phagocytic cells, plain or chromicized catgut, practically irrespective of size, loses tensile strength with great rapidity; (3) when infection is foreseen or when the premature loss of tensile strength in the catgut would be disastrous, removable nonabsorbable tension sutures are indicated as an adjunct to the closure of the wound.

When enucleation was performed the fact that suppuration often followed and that difficulty arose in obtaining complete closure of Tenon's capsule led to the conclusion that the catgut was often unsterile and that its use did not permit complete closure of Tenon's capsule.

The idea of not burying catgut was first brought to my attention when I observed gynecologists (30a) closing abdominal wounds. This principle has been applied to the enucleation operation (6). One needle of the double-armed suture of No. 5 paraffinized black silk is passed through the conjunctiva. The needle is then passed through Tenon's capsule into Tenon's space. A purse-string suture is placed within Tenon's capsule and includes the tendons of the recti; care is used not to overlap the edge of the capsule. The ends of the sutures are then knotted over a rubber tubing and the

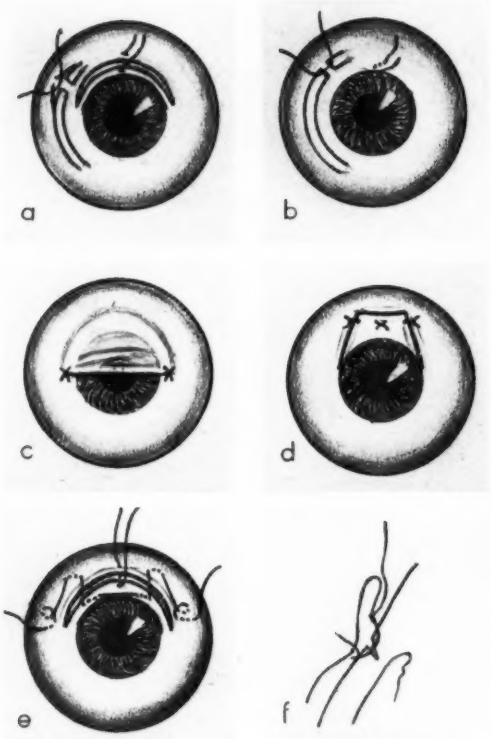


Fig. 6. Methods of closing cataract wounds. a, Williams' conjunctival suture (1867); b, Kalt corneoscleral suture (1894); c, Van Lint conjunctival flap; d, Barraquer (1923) and Green (1923) conjunctival apron; e, Berens running conjunctival and episcleral suture (1925); f, McLean corneoscleral suture (1940).

conjunctiva is closed by means of interrupted plain silk or catgut sutures. Only the deep sutures are removed. This technique has been used in more than 60 enucleation operations and postoperative loss of the implanted foreign substances has been less frequent than when catgut sutures were buried. The plastic implant (10) has been expelled in only 2 cases.

Although surgical wounds have been closed with sutures for years, ophthalmic surgeons have been slow in suturing cataract wounds. However, the use of sutures in this operation has been almost universally adopted in the United States of America since the discussion of this subject before the American College of Surgeons in 1925 by Zentmayer, Posey, Ellett, and the author; at that time there was great difference of opinion in regard to the value of suturing. Ellett championed the Kalt suture; the author the conjunctival episcleral suture; whereas Zentmayer and Posey opposed the use of sutures. At that time none of the surgeons at the New York Eye and Ear Infirmary was employing sutures, except occasionally in complicated cases. Now in the majority of eye hospitals in the United States, sutures are used routinely for cataract extraction and several refinements have been suggested (Fig. 6).

The principle of not using tension in suturing has been applied to cataract wounds for too much tension causes overlapping of the scleral and corneal wound edges.

STERILIZATION OF INSTRUMENTS AND DRUGS

By 1895, chemical sterilization had been replaced by dry heat and steam sterilization, except in the preparation of the skin and of the operating field.

Morax dry heat method. This method is satisfactory for the sterilization of eye instruments. Thoroughly cleansed dry instruments are placed in open boxes in an electric sterilizer (Moria) and the door is left partly open until a temperature of 180 degrees F. (80 degrees C.) is reached, to be sure the instruments are dry. The boxes are closed and wrapped in paper and the door is shut when the danger of retained moisture with resulting oxidation is past. When 335 to 345 degrees F. (155 to 160 degrees C.) is reached, this temperature is maintained for 30 minutes. Sets of instruments may be kept sterile for 1 week. If wrapped boxes are dated, the differentiation of sterile from nonsterile instruments is facilitated. Single instruments and syringes may be sterilized in large glass test tubes closed with cotton. The principal objection to the dry heat method is that several sets of instruments are required.

Chemical sterilization. For the chemical sterilization of instruments M. H. Post has used a solution of alcohol 95 per cent with liquid cresolis compound 2 per cent 2 ounces, commercial chloroform 2 ounces, liquid abolene 2 drams. With these chemicals no rust or tarnish appears on the blades after many days.

Buffering eye solutions for surgical use and their sterilization. To lessen congestion of the eyes in operating it is well to use solutions which are nonirritating. A refinement of general surgical technique is Gifford's method of buffering eye solutions (29). The composition of the acid buffer solution No. 1 is:

Boric acid (anhydrous)	12.4 gm.
Potassium chloride (anhydrous)	7.4 gm.
Distilled water	1000 c.c.

This is suitable for phenacaine and butyn.

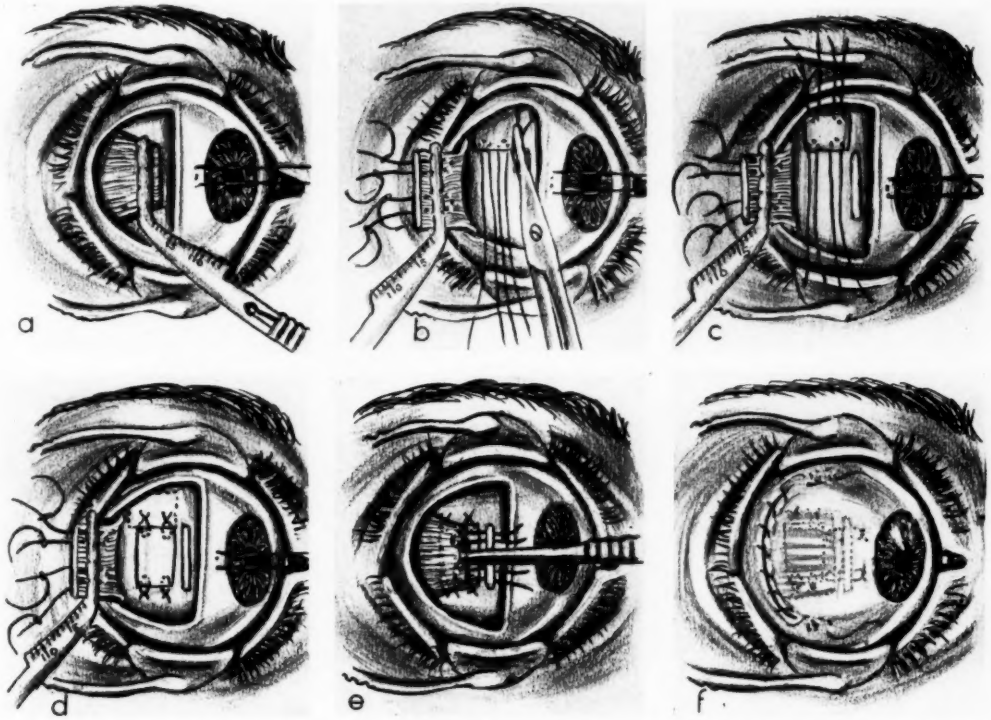


Fig. 7. Transplantation of Tenon's capsule. a, A vertical incision is made along the semilunar fold in order to expose the medial rectus; Tenon's capsule is not disturbed, and a muscle forceps without teeth or pins is passed beneath the muscle; b, the muscle is severed from its insertion, and the fibers lying between the forceps and the insertion are excised if a resection is desired. Two double-armed sutures are passed through the muscle from the scleral surface and then through the holes in the forceps. Tenon's capsule is undermined on one side of the muscle and two double-armed sutures are passed through the border of the capsule. Incisions are made on each side of the sutures. c, Two additional sutures are passed through Tenon's capsule and the graft is freed; d, Tenon's capsule is reversed and sutured with episcleral sutures over the rough scleral area where the medial rectus was formerly adherent; e, the medial rectus is drawn over the graft by means of traction with fixation forceps after the sutures have been passed through the muscle stump; f, the conjunctival wound is closed with a running suture. It is possible at this point to see the muscle and the graft in outline through the conjunctiva.

The composition of the stock sodium carbonate solution is:

Sodium carbonate (anhydrous)	21.2 gm.
Distilled water	1000 c.c.

Gifford's acid buffer solution No. 2, which is suitable for cocaine and epinephrine, is made by adding 0.05 cubic centimeter of the stock sodium carbonate solution to 30 cubic centimeters of acid buffer solution No. 1. His alkaline buffer solution No. 1 is made by adding 1.5 cubic centimeters of the stock sodium carbonate solution to 30 cubic centimeters of acid buffer solution No. 1. It is suitable for atropine, homatropine, pilocarpine and physostigmine. Alkaline buffer solution No. 2 is made by adding 4 cubic centimeters of the stock sodium carbonate solution to 30 cubic centimeters of the acid buffer solution. It is useful in cases of vernal and chronic conjunctivitis.

Preoperative preparation of the conjunctiva. To sterilize the conjunctiva the antiseptics used should be selected according to the organisms found on smear and culture but a 0.25 per cent solution of zinc sulphate is useful as a routine procedure. In certain cases 1:2500 metaphen instilled several times a day has been helpful. Silver as suggested by Bell has been used with apparent success in lessening postoperative infection in cataract operations. Excellent results are likewise claimed by certain surgeons (11), who use no anti-

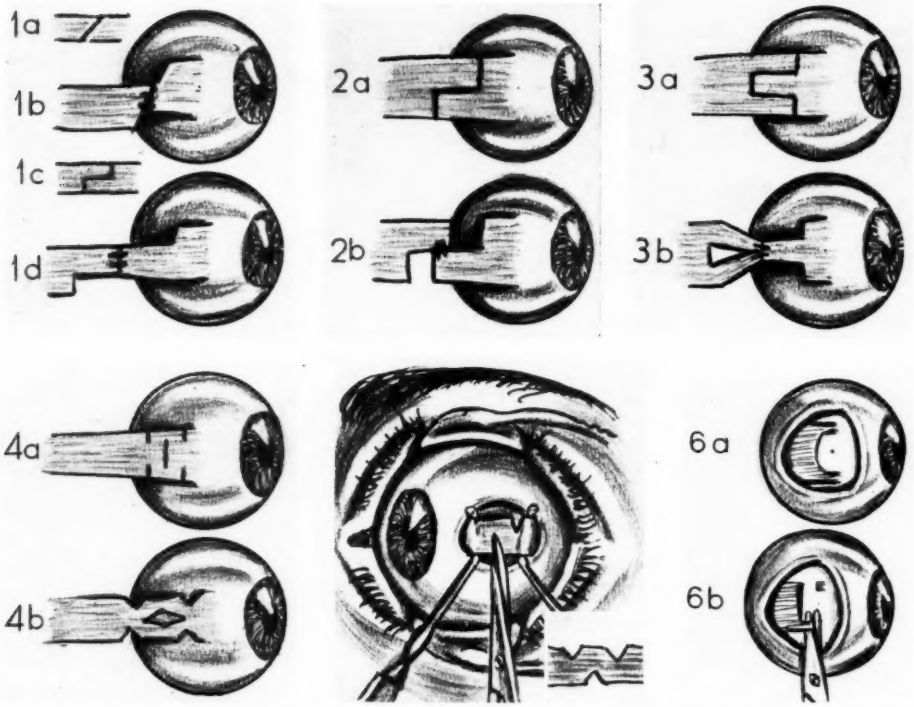


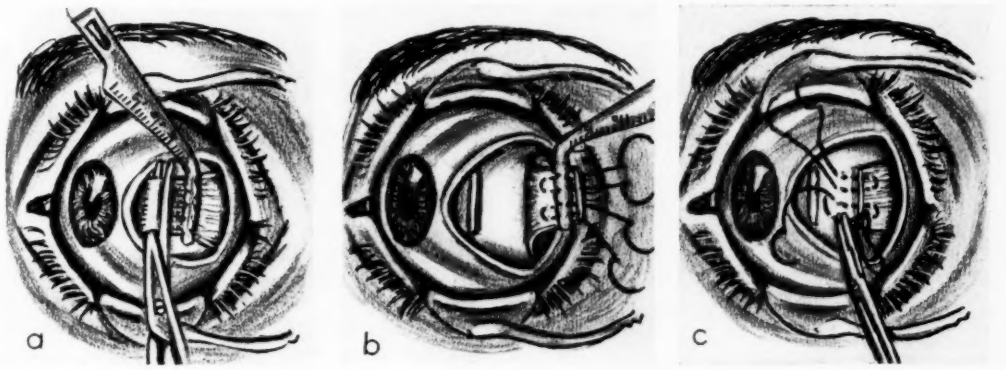
Fig. 8. Tendon lengthening by division of tendon. 1, Stephenson method; 1a, 1b, division and lateral displacement of tendon; 1c, step-division, suturing of upper and lower cut edges. 2, Landolt's similar method: 2a step-like division; 2b, reattachment of muscle. 3, Grimsdale method: 3a, tongue-flap division; 3b, sutures introduced through extreme cut edges. 4, Verhoeff method: 4a, two pair of vertical incisions through one fifth the breadth of the tendon at the upper and lower borders, and a vertical incision midway between the incisions through the middle quarters of the tendon. 5, Todd method: 5a, tendon is stretched between two strabismus hooks, and 2 incisions are made through one-third of the tendon at the upper border, and one incision made through one third of the tendon at the lower border. 6, O'Connor two-stage tenotomy: 6a, a central tenotomy is performed leaving uncut margin of 2 millimeters at the upper and lower borders of the muscle; 6b, after 4 weeks tenotomy of the 2 millimeter bands which were left attached at the upper and lower borders is performed.

septics on the conjunctiva before operation because they assert that asepsis of the conjunctiva is probably maintained by the lysozyme of Fleming when it is contained in the tears in normal concentration. Antiseptics possibly decrease the concentration of lysozyme by increasing lacrimation. Atropine, by producing paralysis of the parasympathetic nerves, diminishes lacrimation and increases the concentration of lysozyme.

MUSCLES

The prevention of adhesions following muscle operations probably originates from the covering of intestinal wounds to prevent adhesions. In eye surgery this principle has been recently applied (7) to the prevention or treatment of adhesions between the muscles of the eyeball and the sclera (Fig. 7). The results in 9 cases have been most encouraging, although in one case the first operation made the condition worse and this has not been rectified. In another patient the first operation also made the condition worse, but a second Tenon's capsule transplant, which was performed at the insistence of James W. White and Daniel B. Kirby, resulted in improvement in motility and appearance.

Tendon lengthening has been used for weakening eye muscles for years, the first attempts following the principles used in general surgery (Fig. 8). However, this procedure has been almost completely discarded in recent years for recession (17, 38) and retroplacement (9) (Fig. 9).



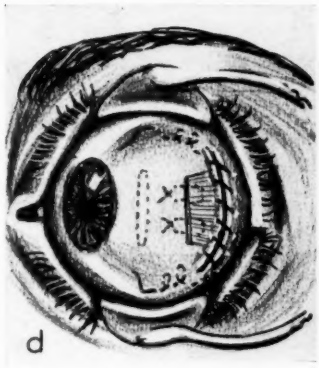


Fig. 9. Retroplacement. a, Severing the tendon at its insertion after applying muscle forceps to the tendon as close to the incision as possible; b, double-armed sutures have been inserted through the muscle and Tenon's capsule from the scleral surface then through the openings in the jaws of the forceps; c, three of the sutures have been passed through the episcleral tissue at the distance from the insertion which was measured and marked by using calipers; d, the sutures of the muscle have been tied. The old tendon insertion is shown as an oval by means of a dashed line. The conjunctiva has been closed with a running No. 0000 catgut suture.

Transplantation. The transplantation of facial muscle or other muscles has been practiced for years. In eye surgery transplantation of an eye muscle was first performed by Jackson when he receded and displaced the superior rectus laterally for paralysis of the superior oblique.

Gifford (30) believes that transplantation of living tendon slips from the superior and inferior rectus muscles offers the best chance of a cosmetic and functional result in paralysis of the lateral rectus muscle.

A brilliant result was obtained by me in one patient (Major F. L.), who had a paralysis of the sixth nerve, and was referred by Dr. Daniel B. Kirby. Transplantation of the lateral half of the superior and inferior recti with Tenon's capsule to the attachment of the lateral rectus, combined with a 6 millimeter resection of the lateral rectus and a 4 millimeter retroplacement of the medial rectus, was performed. Binocular single vision was obtained and he was admitted to the Canadian and American air forces. Before operation his vision was 20–15 in each eye without correction. He had an esotropia of 45Δ for distance and 40Δ for near. At the last examination he measured an esophoria of 10Δ for distance and 5Δ for near. His vision was normal in each eye and no lenses were prescribed. At the time of the patient's first visit, he complained of diplopia and at the last visit he could hold binocular vision a little beyond the midline in the field of action of the paralyzed lateral rectus.

PLASTIC OPERATIONS

With the advent of Listerian antiseptic procedures, it became possible to repair hitherto permanent disfigurements of the body. Some surgeons began to treat these cases by utilizing living bone, cartilage, and flesh. It was World War I that made a specialty of plastic surgery.

Cartilage transplantation. Von Mangold in 1897 first advocated the use of a section of cartilage to support the anterior prominence of the nose. Bone and cartilage are used for the purpose of reconstructing mesodermal structures. Cartilage possesses the lower metabolic rate (66) and unpre-

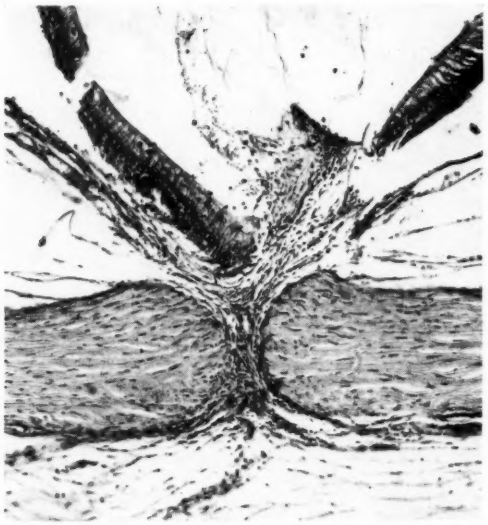


Fig. 10. Episcleral proliferation through electrolysis puncture wound in the eye of a rabbit. Note firm localized cicatrix present after 8 days.

served autogenous cartilage may return to a normal state (Loeb). Autogenous costal cartilage transplantation so far has been used by ophthalmologists mainly for filling in depressions about the orbit, and as an implant after enucleation. Cartilage ("pickled" in 50 per cent alcohol) remains as tolerated dead foreign bodies (homografts) for about 9½ months (53).

Autogenous cartilage from the ribs, survives after transplantation, as living cartilage up to periods as long as 6 years, neither increasing nor decreasing in size. Obtaining the cartilage, however, is not without risk. Therefore, costal cartilage, obtained during autopsy, has been advocated by Straith and Slaughter in cases in which the cause of death is known and in which the deceased person's blood is serologically normal. Middle aged persons are preferred because their cartilage does not present too much fibrous tissue or too much calcification.

Cartilage from the ear is most suitable for reforming the upper eyelid.

Transplantation of fat has been used after enucleation (2) for filling the orbit, for preventing depression around the eye, and in cases of scar adherence to the bone.

Fascia. Fascia has been shown by general surgeons to be a living tissue and has been used for the correction of paralytic mouth deformity and for filling depressions. Fascia is used in ophthalmology for filling in depressions which need not be too resistant to pressure as those in the malar region, not involving the orbital margin. Fascia is used for correcting ptosis (43), for the correction of strabismus (28), to line scleroplastic and keratoplastic conjunctival flaps (57), for paralytic lagophthalmos (75), as subconjunctival grafts (74), and for replacing the tarsus.

Preserved fascia lata is claimed to be as useful as fresh tissue and Ellett (20) has used it for the correction of ptosis with varying results.

Grafts. Plastic surgeons have taught ophthalmologists many ways of using different types of grafts. Although Szymanowski in 1867 wrote the first thorough book on restorative surgery, it was not until 1871 that Reverdin introduced the circular epidermal skin grafts.

The Thiersch graft was introduced in 1886 and proved that comparatively large pieces of skin could be transplanted. These grafts consist of very thin strips of epidermal skin taken from the extensor surface of the arm or the anterior region of the thigh. The Thiersch razor, an ordinary razor or grafting knife may be used to remove the strips but I have found that more uniform and thinner grafts may be obtained with the Padgett (52) dermatome. The technique I have found useful in restoring the socket is as follows: The socket is prepared as advised by Weeks (71) and Wheeler: The eyelids are undermined to the orbital margins. Kerr's dental compound wrapped in a Thiersch graft is inserted after the canthotomy.

Gillies has used the Esser epithelial inlay (22) for contraction of the outer canthus.

Wolfe of Glasgow, 1876, also utilized fairly large free skin grafts. The piece of skin was cut from selected parts of the body, preferably the outer side of the arm. Its size was about one-third larger than the size and shape of the area to be covered. Weeks (72) used the Wolfe graft for restoring the lower eyelid, obtaining the graft from the inner surface of the upper arm. When possible it seems preferable to obtain the skin from the upper eyelid as the color is better.

Pedicle grafts were used by Kaspar Tagliacozzi and described in his book entitled *De Corturum chirurgia per insitionem* (1597). He restored the entire nose by means of a double pedicle flap taken from the arm. Pedicle flaps have been used for coloboma, and the correction of permanent fistula of the eyelids.

Blair and Brown prefer a skin graft of intermediate thickness for certain plastic procedures, for example, the back of the hand not over the knuckles and on the subcutaneous muscles of the face and orbicularis oris and palpebrum.

Blanket grafts. A method of skin grafting which is termed "blanket graft" by which a graft with a total area of 176 square inches is prepared, has been described by McPheeters and Nelson. In their technique a pattern of the area to be covered is made by tailoring a sheet of gutta percha to fit it exactly, and this sheet in turn is covered with the thinnest grafts obtainable with the Padgett dermatome. The individual grafts are then sutured.

There can be little doubt that the use of free grafts by general surgeons inspired the attempts at total (58) and partial (35) corneal transplantation. Usually the grafts have been obtained from an enucleated eye and transferred immediately but grafts from cadavers have been advocated by Filatov. A transplant was taken from the eye of a cadaver 41 hours after its enucleation. In his case the tissue remained transparent during 41 months of observation. Eyes for this purpose are enucleated 2 hours after death and kept in a refrigerator at 5 to 6 degrees centigrade.

GLAUCOMA

There are some points of similarity between intracranial hypertension and glaucoma and the surgical treatment used by neurosurgeons and ophthalmologists. In 1665 D. Julio Sala employed a trephine to drain a penetrating head wound. Who can doubt that the trephine operation for glaucoma really had its inspiration in the work of Sala. Eliott and Fergus were the first to use a trephine for the removal of a segment of the corneosclera in operations for glaucoma.

There is a marked similarity between the Lagrange iridosclerectomy (39) and iridocorneosclerectomy (5) and subtemporal decompression (18). However, according to Hartmann (34), Lagrange developed his technique without knowledge of Cushing's work, although one might surmise that there was a relationship.

Formerly in the treatment of brain abscess, trephination and drainage by means of wicks were employed. Mosher's drain, 1916, was a real advance. This operation may be compared with iridotasis (13) and with the drain operation of Troncoso as well as the seton operation (80) and the Wiener drainage operation. Wiener put a thread between the choroid and the sclera (76).

ALCOHOL INJECTIONS

In 1903, Schloesser used alcohol injections for trigeminal neuralgia. In 1915, Sicard (62) injected alcohol into the nerve-trunk of the median nerve in cases of painful lesions of the nerve plexus. In 1930, Weekers called attention to the sedative action of the intraorbital injections of alcohol. He referred to the work of N. Bruce in 1913, Brady in 1915 and others who showed the value of anesthetics in inflammations.

Ciliary ganglion. Magitot injects 1 to 1.5 cubic centimeters of 20 to 50 per cent alcohol into the ciliary ganglion in cases of iritis, iridocyclitis, glaucoma secondary to iridocyclitis, interstitial keratitis (syphilitic), phlyctenular keratitis in children, and acute glaucoma even with good vision, I have used 1 cubic centimeter of 80 per cent alcohol in absolute glaucoma with high tension and pain. The pain and tension have been relieved in several cases. I inject 1 cubic centimeter of novocain, 4 per cent, with 3 minims of 1:1000 adrenalin in the region of the ciliary ganglion. The needle is left in place, after 5 minutes the alcohol is injected.

For pain and glaucoma, Alexander rejected the resection of the ciliary ganglion and Grueter's injection of alcohol into the orbit around the ciliary ganglion on account of their risk and adverse complications, i.e., paralysis of ocular muscles, perforation of sclera, possible necessity for enucleation, pain. He found that injections of alcohol into the gasserian ganglion gave great satisfaction in neuralgia of the trigeminus, as there were no ill effects.

Fifth nerve and gasserian ganglion. Schloesser, Ostwalt, Levy and Baudouin and Sicard (62) were among the first to inject the nerve-trunk in trigeminal neuralgia. Groves has recommended the injection of the branches of the trigeminal nerve with 80 per cent alcohol. This is done through a long needle thrust into the cheek so as to lie above the sigmoid curve of the jaw, and an endeavor is made to enter the foramen ovale or the sphenomaxillary fossa, in order to inject the actual nerve trunks near the ganglion.

Supraorbital neuralgia. Three cases of severe headaches were treated by Swetlow with relief for 10 to 12 weeks, by alcohol injections of the great occipital or supraorbital nerve.

Sphenopalatine ganglion. Pain produced by keratitis, iritis, glaucoma, and other ocular conditions may be controlled by anesthetizing Meckel's ganglion or by intraorbital injections. In addition to the relief of pain there may also be a decrease in photophobia, blepharospasm, and lacrimation. Magitot's methods of anesthetizing the sphenopalatine ganglion are as follows:

A. Local application—Bonain's solution (cocaine, menthol, carbolic acid) is applied with a cotton pledget either directly or after cocaine 4 to 5 per cent. This application may be repeated every 4 or 5 days. Technique: An applicator, slightly bent, is introduced between the lower and middle turbinates, following the lower edge of the middle turbinate until its posterior end is reached. The tip of the

applicator is rotated slightly outward and is pushed a little further, allowing it to rest on the fossa containing the sphenopalatine ganglion for 10 minutes.

B. Injection of the sphenopalatine ganglion—with novocain injected directly in the sphenopalatine ganglion, through the greater palatine canal, injection should be made in the mouth at the level between the second and third molar, where the velum merges into the gum. Aubin's angulated syringe is used with a 35 millimeter rather blunt needle. Some novocain is injected under the mucous membrane of the mouth; the needle is then pushed into the greater palatine canal (35 mm. deep) and 1 cubic centimeter of a 2 per cent solution of novocain is injected. It is inadvisable to inject alcohol because some cases of necrosis of the maxilla have been reported, probably because the palatine artery was injured.

Spastic entropion. The injection of alcohol for the correction of spastic entropion has been advocated by several ophthalmic surgeons. The skin about the external canthus is painted with 3 per cent iodine, and 0.5 cubic centimeter of a 4 per cent solution of novocain, is injected into the outer fibers of the orbicularis muscle, extending a distance of about 4 or 5 millimeters into the lower eyelid near the margin. The needle is left in place and 0.2 to 0.3 cubic centimeter of an 80 per cent solution of alcohol is usually injected into the muscle. (I prefer 0.5 c.c. of 60 per cent ethyl alcohol.)

INJECTIONS FOR PAIN IN HERPES ZOSTER

According to Secunda, Wolf, and Price in 13 of 15 patients with acute herpes zoster, relief from pain was obtained by injections of 0.5 per cent to 2.0 per cent novocain followed as necessary by nupercaine, Hollander's formula or a modification of it, thus:

Benzocaine	3
Benzyl alcohol	10
Phenol	1
Oil of sweet almond q.s.ad	100

While pain disappeared promptly, it recurred in some patients from 1 to 30 hours later. Injections of novocain and the anesthetic in oil permanently abolished the pain in 7 of 9 patients. The areas of herpetic hyperesthesia are mapped out by pin prick, brush or pinching, cleansed with 95 per cent alcohol and subcutaneously infiltrated with the therapeutic agent until there is total anesthesia.

SCLEROSING INJECTIONS FOR ANGIOMAS

There can be little doubt that the injection of sclerosing solutions for varicose veins (27) and hemorrhoids led to the use of these solutions by ophthalmologists. Forestier who made the first injections recommended sodium salicylate, quinine, and red mercuric iodide. The reaction (venitis) which leads to obliteration and secondary atrophy of the superficial vessels is now usually produced by sodium chloride, sodium morrhuate, monoethanolamine oleate, 66 per cent solution of dextrose.

Malkin has successfully injected hemangioma of the eyelid with sclerosing solutions (e. g., quinine and ethyl carbamate, quinine dihydrochloride, sodium chloride).

ELECTROSURGERY IN THE EXCISION OF TUMORS, EXENTERATION AND DETACHMENT OF THE RETINA

The experiments of d'Arsonval and Oudin led to the use of electrosurgery in 1907 and diathermy was first employed in eye operations in 1911. In 1929, Moers described the use of the diathermy knife for orbital phlegmon. He believes that the advantages of this method are: (1) pus is evacuated without opening blood vessels or lymphatics and (2) the diathermy incision produces sterilization along the line of incision and of the tissues a certain distance from the point of application. Monbrum has given the following indications for coagulation: exenteration of the orbit for a large invading tumor as well as destruction of tumors or other chronic proliferations of the eyelids and the bulbar conjunctiva.

In performing exenteration of the orbit, McReynolds also prefers the electrocautery knife which reduces to a minimum the hazard of spreading the cancer cells.

Diathermy has been most successfully applied to operations for retinal detachment, and the majority of surgeons in the United States of America (8) prefer it. Safar used a diathermy current of about 30 milliamperes, small needles about 1.5 millimeters in length placed over the retinal tear, then over the entire area of the detachment. After all the needles are placed and the current is applied, he removes them, thus allowing free escape of subretinal fluid. Some surgeons prefer the Lacarrere needle, Walker pins, or the Gradle curved needle applicator and about 40 milliamperes of current.

ELECTROLYSIS

Electrolysis, so long used by dermatologists for the removal of superfluous hair, is especially useful to remove cilia. I prefer to use 0.5 milliampere for 1 minute. Electrolysis was first used in operations for retinal detachment by Verhoeff in 1917. In my experience (8) and from animal experiments (Fig. 10) electrolysis makes a more firm union between the retina, choroid, and sclera than does diathermy. In applying electrolysis in the macular region I have found that the delicate platinum

needles of Walker, 1.5 milliamperes for 3 seconds, are useful. I prefer to use the Grieshaber steel needles, 5 milliamperes for 5 seconds, in the peripheral parts of the retina.

SUMMARY AND CONCLUSIONS

Although some surgical practices seem to have originated with ophthalmic surgeons, most of their procedures seem to be adaptations or refinements of general surgical technique. Special consideration is given to the following: anesthesia, incisions, sutures and suturing, sterilization of instruments and drugs, muscles, plastic operations, glaucoma, alcohol injections, injections for pain in herpes zoster, akinesia, sclerosing injections for angiomas, electrosurgery in the excision of tumors, exenteration, detachment of the retina, and electrolysis.

Although Ambroise Paré said we will have to give thanks to God for our humanity and skill, the ophthalmic surgeons should also thank the general, neurologic, and plastic surgeons for much of their success in attaining the hippocratic ideals of ability, grace, speed, and painlessness.

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RECENT TRENDS IN THE SURGERY OF HETEROTROPIA

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THE operative treatment of heterotropia has recently completed its one hundred and second year. On October 26, 1839, Dieffenbach, inspired by Strohmeyer's ideas and following Delpech's technique for tenotomies, performed the first squint operation by cutting the internal rectus of the right eye in a boy of seven. Since then much has been written on the subject. At first there was an almost unbelievable mania for operating on cross-eyed individuals, and tenotomies and myotomies were done by the thousands in all parts of the world, with the inevitable bad results. There followed the usual reaction of skepticism. The improvements in surgical technique by von Graefe and others throughout the nineteenth and at the beginning of the twentieth century did not seem able to overcome that reaction, and in 1905 Haab is quoted as having stated that "the operation for the correction of strabismus is the least satisfactory of all operative procedures on the eyes" (83). Landolt mentioned the fact that an old practitioner and professor of ophthalmology had given the surgical treatment of strabismus up completely on account of its unsatisfactory results. But Landolt himself did not agree with that attitude toward the operative treatment of heterotropia and emphasized that bad results were a consequence of not adhering to the fundamental surgical principle, "Understand the nature of the disease we attack. Understand the way operations work." Much good clinical and surgical work has been done since in the field of surgical treatment of strabismus, chiefly in Anglo-Saxon countries, and Landolt's advice seems to have been followed as much as possible. Consequently, the results of that treatment have improved continuously.

Strabismus, according to William Thornwall Davis, is really a complex of diseases having one common symptom, namely the deviation of the eyes from their parallelism. Better understanding of this complex of diseases is responsible for the establishment of general rules for treatment to be applied intelligently in each individual case. Surgery is a very important part of that treatment, although one should always bear in mind that "to employ the highest type of surgery is but to take a small step toward the production of a physiological result" (Nugent). This small step, however, is in many instances absolutely necessary and it seems to be an accepted rule that when strabismus does not show any improvement after a reasonable trial period of 6 months (Wilkinson) with medical and orthoptical treatment or if such improvements come to a standstill, there is no other alternative but to operate. Duane's statement that "temporizing treatment with prisms and exercises has very decided limitations" should never be forgotten. Worth-Chavasse added to Duane's caution "temporizing treatment must now be recognized for what it is—fiddling while Rome burns."

There does not any longer seem to be serious controversy regarding the necessity for early treatment of strabismus; nor regarding the aim of the treatment—namely, to establish simultaneous binocular stereoscopic vision. It is true too that when operations have to be resorted to, they are but one phase of the treatment, preoperative and postoperative orthoptic medical treatment being equally essential in order to get good physiological results. It is an equally accepted truth that the medical treatment of heterotropia succeeds in greatly reducing the proportion of surgical cases.

As Lancaster has recently emphasized, accurate knowledge of the nature of the extraocular muscles, of their form and functions is of great importance for the complete understanding of the surgical treatment of heterotropia. As he has pointed out, it is essential to know that weakening or strengthening one given muscle is not the purpose of an operation for the correction of strabismus. The real aim of such a procedure is to place the eye in a more favorable position for synergic movements with the fellow eye, to enable simultaneous macular perception, fusion, and stereoscopic vision. One should never forget that there is a great disproportion between the power of each muscle and the energy actually needed for the movement of the eyeball; consequently, the idea of strengthening or weakening simply one muscle cannot prevail.

In order to be able to choose the best surgical procedure, it is of great importance to investigate the nature of each case of heterotropia and never to neglect consideration of convergence and di-

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vergence. Therefore, exact measurements of the angle of deviation are essential. Equally essential is exactness in grading the several types of operations according and in proportion to the amount and nature of each case. The experience of many surgeons has enabled them to establish certain tables in which to each degree of deviation a corresponding number of millimeters of recession, advancement, or shortening, as the case may be, is given. These tables are undoubtedly very useful, but the functional condition of the external muscles taken individually and in their synergical association as well as the many variations of each individual case should be also taken into consideration.

Great importance has been attached of late to vertical deviations, since (White and Brown; Davis; Dickey) their presence or absence is the chief factor involved in the failure or success of surgical treatment. It is widely known that vertical hyperphorias are much harder to deal with, and it is only logical to assume that the same difficulty in fusion found in latent vertical deviation, even after the correction of the lateral defect, will hamper the establishment of fusion which is necessary to complete the surgical results.

It appears to be an accepted fact that whenever possible the operation should be divided between the two muscles concerned in the deviation (Curdy), this being advantageous both from the point of view of the technique and of the end-results.

It seems futile to expect that an operation on the external muscles of the eye can place the deviated eye in complete parallelism to the other eye. It is a well known fact that moving the eyeball by 1 millimeter in any of its meridians will deviate the visual axis by approximately 5 degrees, and with the technical methods at our disposal now it is not possible to grade any muscular operation to a fraction of a millimeter. Thus it is quite clear that it is a surgical impossibility accurately to change the position of an eye to such a fraction so as to make its visual axis parallel to that of the fellow eye. A deviation of 5 minutes of the visual line of one eye in relation to that of the other will cause blurred vision (Fig. 1); consequently, a deviation twelve times as great will render simultaneous macular perception with normal projection completely impossible. The purpose of the operation is to place the deviated eye in such a position that fusion will be rendered possible.

Some well known types of operations such as simple tenotomies, the end-results of which are utterly unpredictable, have been banned. But many other methods have been devised, the excellence of which is questionable. McReynolds, according to Durr and White, according to Spaeth (64), are quoted to have said: "Every oculist suffering with insomnia devises a new operation for squint and all oculists have insomnia." There certainly is no doubt as to the very large number of methods found in the ophthalmological literature for operations on external muscles of the eye with or without special instruments. And many papers dealing with the surgical treatment of strabismus which are found in the journals or presented at society meetings cannot be regarded truly as contributions toward the progress of this branch of ophthalmology. Some of these papers deal with some minor and really unimportant details in the technique. Others tell about the individual preference of the author for this or that type of operation which he uses indiscriminately for all cases. Others devise plans for the choice of this or that type of operation depending entirely upon the number of degrees of heterotropia in each case. Others, still, give statistics of a large percentage of cures, but these cures are only anatomic; and, in some instances, when the proportion of physiological cures is mentioned their small number is an indication of the inadequacy of the methods used. Going through the literature of the treatment of heterotropia one is flabbergasted by the difference in quality of the different contributions, and it is quite surprising to find papers published the same year and coming from cultural centers of equal standing that are so different in their outlook. One will be a well presented and conclusive paper illustrated by a carefully analyzed series of cases of strabismus, in which some patients had and some had not had postoperative orthoptic treatment; and the next will be a brief description of some crude method of increasing the effects of a simple tenotomy.

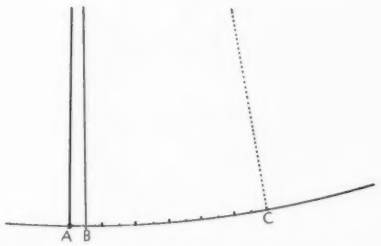

Fig. 1. Points *A* and *B* are 5 minutes apart and a difference of 5 minutes will cause slight diplopia. Points *A* and *C* are 1 degree apart from each other. The most accurate operative methods can be exact to the millimeter, corresponding to 5 degrees.

Recently Harms, Herlyn, and Renner made a survey of a series of strabismus patients in central Europe, who had already been operated on, and found that very few patients indeed could be spoken of as physiologically cured. In an overwhelming majority of cases there was a more or less perfect anatomic cure. As Harms pointed out, this was due to the fact that the approach to the significance and essence of concomitant strabismus is not sound and many ophthalmologists still abide by Wiesel's ideas expressed as follows: "The surgeon performing an operation for strabismus does away with the pathological alterations found in the eye and thus serves cosmetic purposes which are so generally welcomed nowadays."

Experimental pathological investigation in order to verify histologically the result of surgical methods has been done to a small extent. It can be readily understood why such investigation cannot be easily carried further with human eyes; consequently, the source of our knowledge must of necessity remain in the clinical field. Thus it would be of great advantage to the progress of our knowledge if ophthalmologists could be induced to give the subject of strabismus more care, so that so much of their efforts would not be completely lost. Only analysis of the end-results of many well observed cases will enable us to judge the advantages of a particular method, and for that purpose a fixed criterion for gathering the data for such papers should exist. A comparatively large number of instructive papers dealing with the treatment of strabismus and meant for doctors who are not ophthalmologists, and even for the lay public, have been successful in increasing the number of cross-eyed children being given proper care. In the same way possibly something could be achieved to educate ophthalmologists.

In spite of the great difference in standards, by and large considerable progress in the surgical treatment of concomitant strabismus may be noted, and it is to be hoped that with an increasing number of cases coming for early treatment, as a result of the enlightenment of the general practitioner and the lay public, more will be achieved in the near future.

Regarding the surgical treatment of paralytic strabismus, in comparison there has been more progress in the last few years, as can be readily inferred from the increasing number of papers (the majority of them very good), dealing with this subject, which are found in the literature. This growing interest in the surgical treatment of paralytic strabismus is most desirable because, as it has been pointed out by Gifford (28), there are still many ophthalmologists who give the matter little or no attention, and moreover our approach to the subject will undoubtedly benefit from the gathering of new data.

Differences of opinion still prevail to a large extent regarding the choice of the operation for each type of case. This seems to be due more to a lack of proper diagnosis, quite difficult in many instances, than to actual individual disagreements. The paralysis of an external muscle can easily cause a contraction of its opponent or an overaction of its synergical associate muscle in the contralateral eye, and the predominance of the latter or of the former action can give a rather confusing picture. If the real cause of the deviation is not discovered, improper treatment will follow with all of its evil consequences, including the discrediting of a good method.

The exact diagnosis is sometimes really difficult to establish. Sound knowledge of all the muscular functions, more especially in the several directions of ocular gaze as it was emphasized by Vander Hoeve and Roelofs is a condition *sine qua non* of success.

Generally speaking there are already some accepted rules for the choice of the operative method, as Peter has pointed out, and these rules are the result of constant observation. But regarding what can be expected from each type of surgical treatment there is still some controversy (Gifford, Bielschowsky, et al.). The same controversy prevails in relation to the possibility of transplanting the tendon of a lateral rectus to a spot a few millimeters above or below its former attachment for the purpose of correcting vertical deviations (Casten, Mikuni). There is also a difference of opinion regarding the action of transplanted tendons of abducting muscles. Experiments in anima vili (Olmstead, Marguti and Yanagisawa, 72) seem to prove that such transplanted muscles can thereafter have an adducting action, while others (Beard) deny that possibility. Equally controversial is the matter of priority in the surgical treatment of combined vertical and lateral deviations: White (79) is in favor of correcting the vertical deviation first, whereas others prefer to correct both lateral and vertical defects simultaneously. The importance of vertical deviations has been emphasized too (Harms, 33), especially in children in whom its early correction has been advocated (Krueckmann) in order to prevent torticollis with its injurious results in the development of the skeleton. Anatomical findings of absent muscles (Casten) and of muscular bands under the contracted rectus internus (Apple) which cannot be suspected before the operation also have been reported.

I shall now proceed to review the several advances in the surgical treatment of heterotropia reported in the literature on the subject from 1937 up to 1940. The year of 1937 has been chosen because a very complete review of the literature up to that date was published by C. Maynard Wheeler in that year.

The prevailing views on the several aspects of the surgical treatment of heterotropia according to the literature in the last few years follow.

Age at which to operate. It appears that in the United States there is an almost unanimous view regarding the question of age as a limitation for the operation of strabismus. Operative treatment should be resorted to whenever found necessary, if the medical orthoptic treatment did not bring about any improvement after a trial period of 6 months, irrespective of the patient's age.

The principal reasons given in favor of an early operation are: (a) greater response to postoperative orthoptic treatment in younger patients; and (b) the disadvantage of having a physically handicapped child mentally influenced by that handicap (Dunnington).

There are still quite a number of opinions in favor of a late operation, chiefly in Europe. The explanation for those opinions are chiefly: (a) the advantage of operating with local anesthetic, this being only possible after adolescence; (b) the possibility of spontaneous cure before adolescence; (c) the difficulty in securing the parents' permission to operate early. Spontaneous cure appears to be very rare indeed, the straightening of the deviated eye at adolescence proving with hardly any exception only an anatomic cure with binocular vision practically always absent.

Regarding the parents' unwillingness to grant permission for the operative treatment, it is a matter of education, and according to the suggestion of Martin and Nugent, both the medical profession and the laymen should be instructed about the advantages of early treatment, operative or otherwise. Regarding the anesthetic, general anesthesia is finding greater favor in strabismus operations at all ages.

Choice of cases for operation. All cases of divergent concomitant strabismus, not responding in a short time to medical orthoptic treatment, are surgical cases. In convergent heterotropia, opinions vary as to the maximum degree of deviation justifying conservative treatment. Some go as far as to advise surgical treatment for all cases above 8 degrees (Sternberg); others to state that under 15 orthoptic treatment alone is adequate. Here again it is rather hard to establish a fixed limit based on the degree of deviation for operative and nonoperative cases. As long as there is marked and continuous improvement with orthoptic treatment, operative treatment should be postponed. Whenever there is a high degree of hypermetropia great caution is advisable: even if full correction of the existing ametropia fails to correct the tropia immediately, a belated improvement may still be expected and consequently surgical treatment should wait (Dunnington).

OPERATIVE PROCEDURES

There are several types of operations for heterotropia. Some aim at increasing the effect of the muscles, and others at decreasing it. Among the operations of the first group are the advancement of the tendon and the shortening of the muscle, or the combination of both types, as in advancement with resection. The advantages and disadvantages of each group will be discussed later.

The different types of operations should not be used indiscriminately. If individual preferences for a particular surgical procedure are put aside when the preference seems to have no special basis, there are definite reasons for the chosen methods of treatment of the several types of strabismus.

According to Gibson there are three main causes of bad results in the surgical treatment of heterotropia; namely overcorrection, undercorrection, and choice of the wrong type of operation. Hence, it is important to choose the type of operation most adequate according to the exact findings and measurements in each individual case.

Some controversy seems to prevail regarding the importance of measuring the actual strength of each individual muscle in order to choose the operation in the different cases. Lancaster does not pay much attention to the action of each individual muscle, whereas others still attach great importance to it and even go to the extent of testing the strength of the muscle at the beginning of the operation in order to decide the type of surgery ultimately to be used (Jameson).

The relative state of convergence and divergence appears to be of major importance in the choice of the operative method (Maxwell Langdon, 42; Peter, 54; Dunnington). According to Prangen (59) increased esotropia at the near point is a sign of excess of convergence and increased esotropia for distance is a sign of excess of divergence. Conversely, decreased esotropia at the near point is a sign of lack of convergence and decreased esotropia for distance is a sign of lack of divergence. Accordingly, in cases of excess of convergence the interni should be weakened; in cases of excess of divergence, the abductors should be

weakened; in cases of lack of convergence in convergent strabismus, an operation strengthening the externi should be preferred; in cases of lack of convergence in divergent strabismus an advancement of the interni should be chosen; in cases of lack of divergence, strengthening of the abductors is the method of choice.

More and more the idea prevails that the action of the operative treatment should be equally divided as much as possible between the two antagonist muscles of the same eye, in order not to have too much tension in the sutures which might cause ultimate changes in the results (Curdy; Berens, 12; Kirwan). Gibson was led to favor this idea too by the good results observed in cases of very great deviations in which this method of operating simultaneously on two muscles of the same eye had been used.

A careful examination of each individual patient is essential for the proper diagnosis of the actual cause of the "symptom." And this diagnosis is absolutely necessary for the choice of the proper operative method. Guibor classified the several types of strabismus and their respective aspects in the different tests. Thus, the test for visual acuity will spot all cases of amblyopia; testing the movements of the eyeball will show the difference between a pseudoparalytic strabismus and that of heterotropia due to underaction or overaction of individual muscles; the use of atropine rotates the eye inward in the pseudoparalytic and decreases the deviation in the accommodative type. The correction of ametropias with proper glasses will decrease the deviation angle in both accommodative and anisometropic type; measuring the angle for the near-point and for distance enables the separation of the muscular from the accommodative types; the tests for fusion will show a certain degree of fusion in the accommodative type, fusion for larger images in the anisometropic, partial fusion in the amblyopic, and none at all in the fusion type.

When double hyperphoria (Verhoeff) is found simultaneously with lateral deviations it is very important to have that corrected either before or at the same time as the lateral strabismus.

Simple tenotomy. Simple tenotomy nowadays had better be mentioned in the historical part of the surgical treatment of heteropia, for there is no possible difference of opinion regarding the unpredictable effects of this crude and unscientific method. Both experimental work and clinical investigation have proved without any possible doubt how unreliable the method is. A few surgeons still use simple tenotomies, but the only acceptable reason for its use is the fact that it is very simple, lending itself to easy performance on young children. However, the possibility of hampered convergence resulting from tenotomy on the internal recti of young children is one of the principal reasons why the operation should not be used.

In the surgery of divergent strabismus, simple tenotomy of the external rectus is still advocated, but logically a recession would replace the simple tenotomy very advantageously.

Controlled tenotomies. In order to avert the dangers of simple tenotomy, several methods have been devised by which a stitch is passed through the muscle or the tendon before it is severed, this stitch being tied afterward to the tendon stump on the sclera, to the conjunctiva, or both.

Von Blascovics described a technique for a controlled tenotomy and his method has found great favor in central Europe (Harms, 33; Miklos). Von Blascovics' controlled tenotomy is quite an improvement upon the more primitive procedure of simple tenotomy, but neither this method nor any other presented so far can compare with Jameson's recession, the tendon of the severed muscle not being properly attached to the sclera and consequently the final attachment being somewhat uncertain and unpredictable. The favor met by controlled tenotomies can be ascribed to the possibility of subsequent improvement of the results of an operation when overcorrection or undercorrection are found to be present. This is achieved by leaving the sutures tied in a way that allows for the tightening or the loosening of the suture in the first days after the operation. More will be said about this presently.

Weakening of muscular action through other methods than tenotomies. Lengthening of muscles is seldom used any more, but occasionally the method is mentioned in the literature. Samurawkin recently advocated lengthening the muscle by pulling hard at it with a strabismus hook. He associates this with advancement of the antagonist. Central tenotomies are still practiced here and there, but their use does not seem justified since, as it has been proved by the experiments of Watrous and Olmstead, this type of operation is effective only because the postoperative attachments to the sclera of the part of the tendon operated upon bring about a reduction in the arc of contact. Peter has deliberately reduced the arc of contact by suturing the tendon to the sclera some millimeters back of the point of normal attachment. Alabaster with gold sutures pulls the muscle in the opposite direction of its action during the advancement of the antagonist, and Worth-Chavasse places a band of electrocoagulation

not exceeding 1 millimeter at the bottom of a deep groove of the same width with the purpose of converting the contractile portion of the muscle in front of the band into inert tendon, thus reducing the action of the muscle. Walker, who studied histologically the muscles after this sort of diathermocoagulation, found that both the nerves and the muscular fibers are destroyed. By and large these different methods have not met with great favor and too little is known about their real merits.

Recession. Recession is undoubtedly the best type of operation for the purpose of weakening the action of a muscle. Jameson advocates a wide conjunctival incision in the plica semilunaris. Curdy severs the tendon with a knife. Peter (55) recommends great care in the handling of the muscle and thus condemns the use of forceps. With the aid of a hook with which he lifts the muscle first on one and then on the other side, he makes one whipstitch at each side of the tendon before it is cut. Even fanlike spreading of the tendon on the sclera seems to be of great importance for the avoidance of future cyclophoria, and the stitches should be made with proper care in order to ensure uniform attachment.

Recessions are limited by the distance to the equator of the point of attachment of the different muscles on the sclera. Thus 5 millimeters for the rectus internus, 4 millimeters for the rectus inferior, 3 millimeters for the rectus externus, and 2.5 millimeters for the rectus superior seem to be the maximum that can be receded. In the case of larger eyes (the diameter of the cornea according to Priestley Smith being possibly the best index to judge about the size of an eye), 1 to 1.5 millimeters more can be allowed for each muscle. It has been claimed that even with larger recessions no ill results such as lack of convergence have been found, and apparently with the rectus externus more liberties can be taken, but on the rectus internus the maximum limit of 6 millimeters should not be stepped over. According to Jameson a 5 millimeter recession of the rectus internus will correct 20 to 25 degrees, and the recession of the rectus externus corrects one-third of that. According to Peter (54) only 12 degrees' correction can be expected from a recession of 6 millimeters, whereas 25 degrees can be expected if the recession is combined with advancement. Results vary considerably according to individual variations of the muscles. As a rule about 5 degrees for every millimeter of recession can be estimated, if the antagonist is operated on simultaneously.

Advancement. This type of operation meant to enlarge the arc of contact is still in great favor (Wheeler) although its results have been questioned and some controversy has arisen regarding its action. Duverger, quite some years ago, experimenting on rabbits found that after some time the advanced tendon finds itself attached to the former stump, in which case the advancement would only act through the shortening of the muscle. Prangen and Horay are of a similar opinion regarding the results of advancements, but Jameson believed that the muscular fibers are still active and can take action even when they are embodied in the attachments to the sclera. Peter is in favor of advancements because he finds that by including the capsule and the conjunctiva in the advancement about 5 to 10 degrees more can be corrected with this type of operation.

Apparently advancements will not correct more than about 15 degrees (Wheeler) except if associated with recession of the opponent. The possibility of using advancements for the purpose of correcting simultaneously vertical and lateral deviations has been considered, but an agreement does not seem to have been reached so far. The majority of papers dealing with advancement merely add details of new techniques, chiefly in the sutures. The operation lends itself to ulterior changes in the sutures for the purpose of correcting surgical defects during the first few days after the surgical procedure.

Resection. Reese's method nowadays finds great favor. The effect of the operation is that of shortening the muscle and sometimes it has been used combined with advancement in order to increase its action. Great care has been taken to make the sutures more effective and to make them safer, by attaching the muscle to the conjunctiva before it is severed. The anchorage of the suture on the tendon stump has been improved too, and several new techniques have been described to that effect. As in all operations on the external muscles, the trend now is to make a large conjunctival incision in order to be able to operate freely on the muscle.

Tucking. In order to obviate the undesirable attachments above or below the previous point of insertion a tucking operation, in which the muscle is not severed at all, was devised some time ago.

An argument raised against the tucking methods, first advocated chiefly by Burch and Grant, is that they are not very exact, as considerable stretching of the muscle fibers takes place during the first days after the operation and that consequently it is very difficult to know how much should be tucked in order to have dependable results. Possible necrosis of the muscle, due to strangulation of the blood supplying vessels, has been mentioned too. But the method has gained

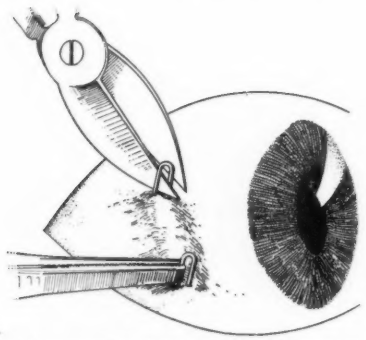

Fig. 2. Myocampter silver ring should be cut as near as possible to the conjunctiva, first where the scissors are and then where the forceps appear in the illustration. The two severed ends can then be easily removed.

much favor in spite of this, and in the hands of those who sponsor this type of surgery the results have been very good. If the tucking is performed simultaneously with a recession, there will not be so much pull on the sutures of the tucked muscle, and consequently less stretching. Apparently not more than 20 degrees can be corrected with tucking. The least that can be tucked to get any effect at all is 8 millimeters (von Blascovics).

Several changes in the technique of the tucking operation have been presented, some advocating the use of instruments (tuckers) and others, only stitches. Recently a method was described providing for an anchorage of the muscle on the sclera near the limbus (Bardanzellu).

The tucking of the muscle jointly with the conjunctiva has been advocated, too, in order to strengthen the operation and to render it bloodless. This has been achieved with ordinary stitches (Szymanski) or with a silver ring in the myocampter of Barraquer or Lacarrère. According to Bristow the myocampter is an improvement of Briggs' instrument presented to the Section of Ophthalmology of the American Medical Association back in 1909, and Otis Wolfe gives testimony to Briggs' priority by stating that during one of his visits to Barcelona, he showed Barraquer Briggs' instrument and that later Barraquer sent him his model. According to Wolfe, Barraquer never claimed priority for this method.

Myocampsis met with considerable favor in the early thirties. Later Hubert and Lebas advocated exposing the muscle first, and then shortening it with the myocampter. This renders the method much more dependable. About 10 millimeters' shortening can correct up to 20 degrees, if a recession is performed simultaneously. Avizonis investigated the pathology of muscles after myocampsis, and found the following changes in the strangulated part of the muscle; cyanosis, hemorrhages, and some necrosis; and Jacqueau reported a case of repeated cyst-like growths on the conjunctiva over the tucked muscle after myocampsis. Removal of the silver ring about 1 month after the operation is sometimes rather difficult, as the ring is completely buried in the conjunctiva. In such cases, after the ring is uncovered each end should be held with a simple forceps and the ring should be cut apart as is shown in Figure 2 (Alvaro, 1).

"Cinch operation" (O'Connor). O'Connor's cinch operation was devised in 1911 and only gradually did it become extensively known. From San Francisco, where it had been used for a long time, it spread gradually throughout the United States and in the last years to Europe. Everywhere it has been welcomed with marked enthusiasm. Barkan's statement about this method, calling it "the most perfect mechanical means of straightening an eye at any age," is one of the many which indicate the enthusiasm so many ophthalmologists have shown for the "shortener" operation.

The advantages of the method are chiefly the absence of sutures and of severance of the tendon. It has been pointed out by some surgeons (Wheeler) that during the first days after the operation there is a rather strong reaction in the eye operated upon, but this has been denied by others (Appelman). About 10 millimeters is the maximum that can be shortened.

Smukler described a needle, 1¾ inches long, made of 14 gauge wire, which he uses for winding the dermal suture round the strips of the muscle. He uses special grooved hooks to keep the strips separated for the insertion of the suture. The muscle is dissected as far as the equator and the dermal sutures should be placed at a certain distance from the point of attachment in order to prevent too much pull on the muscle fibers. Not more than 8 dermal sutures should be used. Cementing both ends of the dermal suture bundle with a special metallic cement is a method advocated by both O'Connor and by Smukler. The sutures should be left for about 2 weeks.

Methods for correcting after effects. Apart from the controlled tenotomies, which lend themselves to further changes in the position of the eye a few days after the operation by tightening or loosening the suture, some methods have been devised of late to enable the surgeon to perform an after correction, if the results do not seem to be satisfactory in the first few days after operation. Harms (33) describes a new method of advancement in

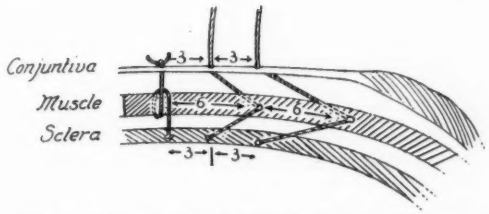

Fig. 3. Diagram showing technique of the Harms controlled advancement operation.

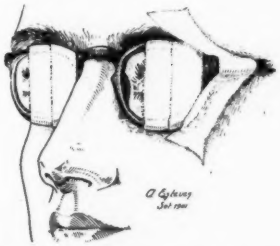

Fig. 4. Von Blascovics' method for subsequent correction during the first 5 to 12 days after the operation.

which he puts in two extra sutures through conjunctiva, muscle, and sclera and again through muscle and conjunctiva, and placed in such a way (Fig. 3) that by tightening them soon after the aperation it will be possible to shorten the already odvanced muscle still more, thus increasing its action. Baudot described a somewhat similar method for the same purpose.

Von Blascovics, as far back as 1922, in certain cases in which slight changes in the position of the eyes (up to 5) were still desirable, had used after operation a special dressing compelling the eye to be in extreme adduction or extreme abduction. The principle of his method was to force the eyes in a certain direction, so that the new attachments would take place in that position. Strebel and Goldman have advocated the use of that method. Instead of von Blascovics' special dressing, ordinary glasses covered with simple adhesive can serve the same purpose (Fig. 4).

Methods for correcting bad operative results. Patients previously operated upon and in whom there is still some heterotropia should undergo the same careful examination as any other case of strabismus, in order to determine the proper methods of treatment at the proper time. In the case of previous recessions or tenotomies a similar operation on the antagonist is not advisable in order to avoid any degree of proptosis. For certain cases in which the ill results have been caused by unwished for adhesions between the muscles and the eyeball, Berens (11) has devised a special technique: he inserts between the adherent muscle and the sclera a transplanted piece of Tenon's capsule, taking care to turn the transplant over, so that the side which was formerly turned to the sclera, will now be turned to the muscle, thus averting the danger of renewed attachments between muscle and sclera. Capsular advancement has been found very useful in cases of paralysis due to previous simple tenotomies.

Divergent strabismus. As a rule there are no special methods for the treatment of divergent strabismus, the same general principles mentioned for convergent concomitant heterotropia begin equally prevalent. Thus an accurate diagnosis of the nature of the deviation in each case is absolutely essential so that one may choose the best method. Furthermore, recessions of the external recti will be justified only in cases in which there is normal convergence, as has been pointed out by White and Brown (80). Coppez goes so far as to recommend complete tenotomies of the external recti, an operation which he otherwise condemns. But even on the external recti, tenotomies are not very satisfactory, and if weakening of the external is desired a recession should be resorted to. Cass is in favor of bilateral advancement with resection of the recti interni. Dunnington too favors a generous strengthening of convergence through a proper operation on the interni.

White and Brown (80) emphasize the importance of vertical deviations in the success of the operative treatment in divergent strabismus, as well as in the convergent. Hypertropia should be corrected preferably before the management of lateral deviation, but in some cases, when it is impossible to discover the vertical deviation with the necessary accurateness, it is justifiable to correct the lateral deviation first. In some cases it is possible to correct both deviations, lateral and the vertical, simultaneously. Generally it is the inferior oblique which is responsible for the vertical deviation, and in such cases a tenotomy or recession (von Blascovics) of the inferior oblique is the method of choice.

Cass calls attention to the fact that operative results are very deceptive in divergent strabismus, and in many cases immediate good results are followed in a short time by a relapse. Early operation is advisable in all cases of alternating strabismus and in those in which there is improper adjustment.

Paralytic strabismus. The possibility of re-establishing binocular single vision, even if this is limited to a very small area in the field of fixation,

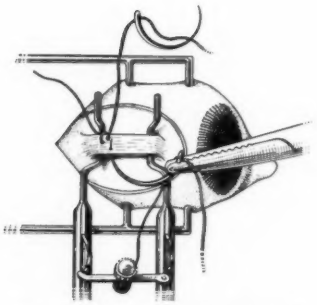

Fig. 5. Gutzeit's muscle speculum.

is welcomed as a blessing by the majority of patients. This fact, recently emphasized by Gifford (27), shows the importance of the surgical treatment of paralytic strabismus. The knowledge of conditions of binocular vision before the onset of paralysis is essential for the choice of the surgical method in each case, and the use of prisms after the operation in order to correct small defects and enable simultaneous macular perception is of equal importance.

An accurate diagnosis of the nature of each paralysis, including a minute investigation of the functional condition of each muscle and of the synergic action of all muscles involved in the movement of the eyes in the several directions in the field of fixation, is of paramount importance for the choice of the surgical method in each case. According to Bielschowsky, especially in the case of vertical deviations, the following questions must be answered before a decision is made as to if and how any kind of paralytic strabismus may be surgically corrected: (1) Does the vertical deviation increase in looking up, or in looking down? (2) Is it different in the right and left halves of the field of fixation? (3) Are the double images of contours parallel in the whole field of fixation, or only in a certain part, being inclined toward each other in the other part? (4) Does the tilting of the head around the sagittal axis without changing the direction of the visual lines influence the magnitude of the vertical and the meridional deviation, and, if so, in what manner? The answers to these questions will enable one not only to differentiate between a true paralytic strabismus and a nonparalytic heterophoria but also to discover which muscles are involved—whether those which are paralyzed or those which have developed an overaction due to secondary contracture.

The surgical treatment of paralytic strabismus should be resorted to only after 6 months have elapsed after the inception of the paralysis without any signs of recovery (Bielschowsky); but afterward early treatment is advisable in order to avoid contractures of the antagonist.

The operative treatment should be directed, whenever possible, toward increasing the efficiency of the paralyzed muscle as it should be remembered that, according to Sherrington's demonstration in 1893, the lengthening of an antagonistic muscle under normal conditions should not be regarded as a passive stretching produced by the contraction of the agonist, but is really due to an active relaxation that takes place even if the agonist does not function at all. It is now recognized, therefore, that it is not possible to improve the function of a paralyzed ocular muscle by means of weakening its antagonist alone. On the other hand, Landolt's assumption that when shortening of the paralyzed muscle proved insufficient the contralateral homonymous status of the shortened muscle in one eye should be strengthened too, does not stand good any more in cases of long standing paralytic deviation with secondary contractions. Landolt very rightly opposed tenotomies and that is possibly the explanation for his policy. Recessions, however, not bringing about the poor results of simple tenotomies, enable us to increase the effect of the shortening operation on the paralytic muscle by relaxation of the pull of the antagonist. In some types of paralytic strabismus strengthening of the paralyzed muscle is technically difficult and weakening of the direct antagonist is not enough or may even have a somewhat unexpected result, due to an overaction of contralateral muscles of synergical action to the paralyzed muscle.

Especially in cases of paretic vertical muscles there are other factors to be taken into consideration whenever parallelism of the eyes is to be reestablished in the largest possible area of the field of fixation by means of an operation. Thus not only the overaction of the contralateral associate has to be considered as moving the eye vertically, but its adduction or abduction and especially its conclination or declination are of great importance.

As an example of the complexity of matters regarding paretic vertical muscles Bielschowsky discusses the subject of inveterate trochlear paresis. As the strengthening of the paretic muscle is difficult, there might be a possibility of improvement of the vertical deviation by the weakening of the rectus superior of the paretic eye. But this would be only in a very limited area of the field of fixation, the effect of this operation being less in the lower part of the field—where the vertical defect had been greater before—whereas in the

upper part of the field of fixation—where there had been only a small vertical deviation, or none at all before the operation—there will be an overcorrection in the sense of a contrary vertical deviation. In the lateral movements results are still worse as the vertical position of the paralyzed eye is dependent upon the oblique muscles, when the patient looks toward the healthy side, the vertical deviation increases in proportion to the increased turning of the paralyzed eye, and conversely decreases when the patient looks away because the vertical position of the averted eyes is influenced by the vertical recti. After recession of the superior rectus there would be an increased deviation both in adduction and in abduction. Still more unsatisfactory is the effect of the recession of the superior rectus on the rotation of the eyes. Both the superior oblique and the superior rectus rotate inward, and consequently weakening of the superior rectus will increase the disclination. Advancing the inferior oblique (advocated by Landolt) would likewise cause a more pronounced disclination, and would improve parallelism only in the lower part of the field, but not in the center, as this muscle is inadequate in the nasal quadrant of the lower half of the field of fixation.

Best results show recession of the inferior rectus of the contralateral eye. This equalizes the function of the associated depressor muscles in the two eyes. If a tenotomy is performed there may be an overcorrection in looking down, but a recession can graduate the weakening of the inferior rectus so that no such results will ensue. It should be remembered that the left superior oblique and the right inferior rectus are associated in depressing and turning the eyes to the right. The left superior rectus turns the upper part of the cornea toward the right of the patient (internal rotation) and the right inferior rectus turns the upper part of the cornea to the right too (external rotation). If the left superior oblique is paretic the upper part of the cornea in the left eye will move to the left (outward). By receding the inferior rectus of the right eye the muscle is weakened and consequently the upper part of the cornea will be turned to the left (inward). Thus the vertical lateral and rotating elements will have been corrected.

Paralysis of the rectus internus. References to surgical treatment of paralysis of the adducting rectus are rather scanty in the literature. Shortening of the rectus internus and simultaneous recession of the rectus externus are generally advocated. Both Jackson and Peter (54) dissect the internal halves of the superior and inferior recti and transplant them to the point of insertion of the rectus internus. Several cases have been reported, mentioning good results, of the transplantation of the superior oblique to the point of attachment of the rectus internus (Wegener), shortening of the rectus internus and recession of the antagonist being performed at the same time.

Paralysis of the rectus superior. An advancement or shortening of the superior rectus has been advocated. O'Connor's cinch operation after tenotomy of contralateral inferior oblique, if this proves insufficient, has been used for that purpose. Peter advances the rectus superior and transplants the upper halves of the tendons of the rectus externus and rectus internus to the new point of attachment of the superior rectus. An advancement attaching the tendon a few millimeters temporal to its previous attachment has been mentioned by Peter too (54). When there is an overaction of the inferior oblique of the contralateral eye, this muscle should be operated on, either by receding it, according to Rugg-Gunn's method, whereby it is reattached to the periosteum about 6 millimeters from its normal insertion, or by a simple tenotomy.

White (77) favors a careful myotomy of the inferior oblique of the contralateral eye and, if this proves insufficient (Gifford, 27), an advancement and resection of the paralyzed muscle. In cases in which even the combination of these two methods is not able to correct the deviation, a recession of the rectus inferior on the paralytic eye should be resorted to. Both Dunnington and White (79) agree about the choice method being either the advancement of the rectus superior or a tenotomy of the inferior oblique of the contralateral eye. When the paralytic eye is used for fixation, there is an overaction of the synergical muscle of the other eye, and tenotomy of the contralateral inferior oblique is to be favored, and, conversely, when the good eye is used for fixation and no such overaction exists, an advancement of the paralyzed superior rectus should be performed. Operations on the superior rectus have the disadvantage of causing a disturbance of the movements of the upper lid and diplopia in the lower field of fixation.

Paralysis of the rectus inferior. An advancement with resection of the paralyzed muscle seems to be the method of choice. If there is an overaction of the superior oblique, a recession of the trochlear of the contralateral eye has been suggested (Berens), and if there is a spasm of the direct antagonist, a recession of the superior rectus. Wiener suggested severing the inferior oblique close to the sclera, reattaching it nasalward from the attachment of the inferior rectus. Casten

reported good results in a case of congenital absence of the inferior rectus, after having transplanted the external rectus to a spot midway between its former attachment and the insertion of the inferior rectus. Extorsion and depression of the eyeball were thereby achieved. Casten advocated simultaneous tenotomy of the inferior oblique if found necessary. Peter advocated the advancement of the inferior rectus attaching it a few millimeters temporalward (and obviously nearer to the limbus) from its former attachment. Bartels, in a case of absence of the inferior rectus and fibrous band of the superior rectus, tenotomized the latter and pulled the eye down with sutures on the limbal conjunctiva tied on the skin of the lower lid.

Paralysis of the rectus externus. This appears to be one of the most common kinds of paralytic strabismus. Advancement or shortening of the external rectus and recessions of the internal rectus have been advocated.

A simple tenotomy of the internal rectus combined with special stitches meant to pull the eye toward abduction has been described by Vogt. The Hummelsheim type of operation with several improvements in its technique has been favored lately by Gifford (28) Beliaev, Goodman, Lancaster, Alvaro (1), and several others, with fairly good results. Gifford reports abductions of 5 to 35 degrees after the operation. O'Connor, instead of using the external halves of the superior and inferior recti, transplants the internal halves. Wiener prefers to sever the rectus externus 15 millimeters from the sclera, split the scleral part in two horizontal halves, and transplant the superior and inferior to the superior and inferior recti.

There is some controversy regarding the way in which the Hummelsheim type of operation works. Some, as Bielschowsky and White (79), believe that results are due mostly to the recession of the overactive rectus internus and White is rather conservative about disturbing the vertical balance, although Gifford (27) has never noticed any change in vertical balance after operations of this type. Spaeth (64) mentioned the results of experimental work done at the Graduate Hospital in Philadelphia according to which the action of the muscular slips is merely that of stays, thus permitting the tension of the other abductor muscles to act whenever reciprocal relaxation of the abductors occurs. Meyer, using indiscriminately the nasal or temporal strips of the superior and inferior recti, stresses the importance of careful dissection in order to prevent too much pull on the sutures. Worth-Chavasse still favors bilateral recession of the internal recti, but that method does not seem to be favored by the majority any longer. Apple calls attention to the fibrous tracts appearing under the contracted internal rectus, which have to be severed in order to get good results.

Paralysis of the superior oblique. Next to abducens paralysis, this is the most common of ocular muscle paralysis. Bielschowsky calls attention to the fact that trochlear paralysis has become more common in the last 30 years and explains this by the more frequent operations of the Killian type, in which the trochlea is easily loosened. Paralysis of the superior oblique causes some form of torticollis, and therefore an early operation is advisable, especially in children.

Von Graefe and Alfred Graefe quite a long time ago had devised a surgical treatment for trochlear paralysis which was abandoned for many years and has now found general favor again, namely tenotomy (now substituted by recession) of the inferior rectus of the contralateral eye. With this method, as it was recently mentioned by Berens, Dunnington, McMullen, White, Arganaras, Marx, and Pincus, results are quite good, although when the patient looks down, the paretic eye is too high, and, conversely, too low, when the patient looks down and away, as it was mentioned recently by Messmann. Recession of the inferior recti has the disadvantage in many cases of causing a certain degree of ptosis of the lower lid. In order to prevent this, a careful suture of the conjunctival wound is essential. Bielschowsky prefers not to tie the sutures of the receded tendon, in order to be able to tighten or loosen them according to results obtained in the next few days.

Tenotomy of the inferior oblique of the same eye is favored too (Ploman) and, according to Spaeth, Duane and Bielschowsky, it should be used chiefly when there is an associated exophoria. The method formerly described, of recession of the inferior rectus of the contralateral eye, is the method of choice when there is esophoria. White favors operating on the contralateral inferior rectus first, and then, if necessary, on the inferior oblique. Gifford, on the other hand, prefers to operate on the inferior oblique first. Dunnington, Messmann, Borsotti, and others favor tenotomy of the inferior oblique only when there is a strong secondary contracture.

Jackson's method of transplantation of the superior rectus was recently favored by Vasquez Barriere, and Savin still favors the method, now generally abandoned, of recession of the superior rectus.

The method advocated by Landolt, of advancing the inferior rectus, has been equally abandoned. Wheeler devised an operation to shorten the paralyzed superior oblique, but its technique seems rather difficult and its use has been discouraged (Peter, 54). Aurand dissected strips of the external and inferior recti and attached them to the sclera at a distance of 3 millimeters from the limbus at the 7.30 meridian.

Paralysis of the inferior oblique. An advancement operation for the inferior oblique has been described by Wheeler. The muscle is detached from the orbit, pulled out, and sutured to the cheek bone. Recession of the superior rectus of the contralateral eye has been advocated by White and Berens.

Bilateral paralysis of homonymous muscles. Handling of bilateral paralysis of homonymous muscles is rather difficult. According to what has been published so far (White, 78), bilateral paralysis of the rectus superior, when it is predominant in one eye, calls for tenotomy of the inferior oblique on the less paretic eye, and according to the result shortening of the superior rectus of the lower eye or tenotomy of the inferior oblique of the other eye. When the patient uses constantly only one eye for fixation (generally it is the more paretic eye), the external rectus of the deviated eye should be operated on by performing an advancement or recession according to the lateral deviation in each case and a tenotomy of the inferior oblique. When one or the other eye is alternately used, bilateral tenotomy of the inferior obliques and in mild cases bilateral shortening of the superior recti should be performed. Whenever bilateral paralysis of the superior recti is almost complete, care should be taken not to touch the inferior obliques, in order not to weaken the elevators entirely.

For bilateral trochlear paralysis Jaensch prescribes recession of the inferior rectus on one eye followed by a similar recession on the other eye if necessary, the second operation depending upon the results obtained in the first.

ANESTHESIA

As in other branches of surgery, the latest developments of anesthesia have done much toward improvement of surgical treatment. Possibly the favor enjoyed by the simpler and cruder methods, the results of which were so unsatisfactory, was chiefly due to the lack of proper methods of anesthesia. There is no doubt about the influence of anesthesia on the opinion of many ophthalmologists as to the minimum age at which to operate on a child with strabismus. General anesthesia was not favored in the older days because during the operation the deviation could not be seen, it was claimed, and consequently the surgeon had nothing to gauge the operation by. Lately however, as has been pointed out by Dunnington, accurate preoperative examination of the patient permits establishing a definite plan beforehand.

Peter (55) favors general anesthesia in all cases, as he believes that local anesthesia is always responsible for some degree of edema which may cause important landmarks to become obscured. Anyway for children under 12 and for those adults whose temperament or disposition prevent them from being co-operative with the operator, general anesthesia is essential.

For general anesthesia the use of ether, vinethene, diethylic ether, nitrogen peroxide, ethylene, cyclopropane (the two latter are inflammable) has been advocated. Magill's tracheal tube should always be used in order to keep the operative field unobtruded (Prangen, 58). Morphine sulfate 0.01 gram and atropine sulfate 0.0004 gram hypodermically, should be given about 30 minutes before general anesthesia.

Evipal, pentothal, and avertin are very useful too, but in most instances a small amount of ether will have to be added. Barbiturates are generally used as preoperative sedatives the night before, and on the morning of the operation both for general and for local anesthesia.

When local anesthesia is used, instillation of anesthetic drops, the gauze pack (Meller), and injection into the muscle sheaths will be found insufficient, and block anesthesia will have to be resorted to. But as it has been pointed out (Weill, Bressler) local anesthesia is unsatisfactory in many cases, especially in the case of undue traction of the muscles and tendons with the hook. The combination of local and general anesthesia has been favored too, with the purpose of reducing the amount of general anesthetic which will be necessary for the operation.

INSTRUMENTS

Many instruments have been built for the particular purpose of rendering one or more phases of a certain type of operation easier, and each operator becomes attached to the type of instruments he is used to. Lately new instruments have been perfected, and the use of others introduced. Thus, Spaeth (65) emphasizes the importance of the lids of the speculum covering the cilia to prevent tiny clippings falling into the wound. For the same purpose Durr uses a sterile rubber sheet in which he makes a slit to insert the speculum, the rubber tissue covering the eyelashes completely.

For measurements of the number of millimeters in advancement, shortening resection, or recession operations, Berens built a special caliper on which the distance between the two points is easily readable, and Green described another model one point of which is very thin and guarded in order to enable easy fixation with little traumatism and no danger of perforation, the other bladelike end of the instrument being meant for marking the sclera with gentian violet or fuchsin.

Tendon spreaders taking the place of the two hooks to be held by an assistant were built by Wurach in Berlin and by Grieshaber in Switzerland after the patterns of Streiff and Schweigger-Gutzeit respectively. Similar to these tendon speculums is the bodkin described by Lodge made of thicker stainless steel wire. The handle and the hook with its terminal eye are ground to the original gauge, but the middle third is forged into a grooved director curved on the flat. The bodkin is meant to put the extraocular muscle at rest and render it more accessible to sutures.

SUTURES

A rather large number of methods for the operative treatment of strabismus have been devised just because the existing sutures were found to be unsatisfactory. Lancaster back in 1901 showed, by his experimental work, exactly how much tension was necessary to pull the simple sutures which were used in those days through the muscle fibers, and the results were not very encouraging. Since then several more reliable types of sutures have been described, such as the stitches zigzagging through the muscle (Lancaster Thompson), Ziegler's "whipstitch," and the mattress suture.

By means of a double armed thread a great number of suture may be made with but one thread; according to Jameson all other things being equal it is best to be able to bring about the apposition of all the tissues with one single suture. Fanlike spreading of the tendon on the sclera, however, is essential, and care must be taken that the sutures keep the tendon in proper position. Strangulation of all the muscular fibers should be avoided by all means, and for that purpose the central part of the muscle should be left free of sutures (Lancaster). The violation of this principle is responsible for many bad results, which change a tucking operation into a tenotomy, the adhesions of the muscle and the capsule to the sclera at a point where the sutures rest on the sclera, being responsible for a less catastrophic result and for the still disappointing *status quo* (Spaeth, 65). The careful handling of the muscles is just as necessary, and forceps should be applied only on those parts which are intended for resection.

The fact that silk could be used without any misgivings in buried sutures (Lancaster) made silk sutures more and more popular in the early thirties. Lately, however, improvements in catgut, rendering it more reliable as to sterility and endurance (10 or more days without resorption and causing little reaction) and the appearance of atraumatic needles have turned the tide so that today catgut is gaining more in favor. Generally No. 000 catgut is used for resections and advancements and No. 00000 for recession and conjunctival sutures (Prangen, 58).

According to Muegge, silk should be waxed before it is used (7 parts of yellow beeswax, 1 part of almond oil, 1 part of salicylic acid—Peter, 55). For advancements on the lateral muscles twisted silk No. 4 or braided silk No. 1 should be used, for the vertical recti, twisted silk No. 2 and for conjunctival sutures, twisted silk No. 1 (Peter, 55).

Scleral sutures have become commonplace, and scleral perforations formerly a formidable occurrence are really rare (Butler).

SUMMARY AND CONCLUSIONS

The large number of operative methods and the almost infinite variations of sutures are an indication that, as it has been stated by C. Maynard Wheeler, "There is no unanimity of opinion as to the proper handling of strabismus. Comparably favorable end-results can be achieved by several methods. The procedure of choice for any surgeon is the one with which he is most familiar and in the performance of which he is most skilful," provided of course the right type of operation for each case has been carefully chosen.

Regarding immediate postoperative dressing there appears to be some slight individual variation. Binocular occlusion for at least 2 to 7 days is almost generally accepted. Barraquer's occlusion bandage seems to be most comfortable to the patient.

Complications are rare. Butler in 30 years lost only one eye, due to panophthalmitis, because of infected catgut, and Kiehle and Henton in 286 operative cases had only one eye complicated with uveitis. Against local reactions, foreign protein has been advocated (Spaeth, 64) and recently sulfanilamide has given good results when administered orally and locally. The local use is conditioned by its solubility so that enough concentrated solutions can be used. For that purpose natrium-sulfanilacethylamide of which 30 per cent solutions can be easily obtained shows good results.

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THE 1941 CLINICAL CONGRESS

LELAND S. McKITTRICK, M.D., F.A.C.S., Boston, Massachusetts

THE Thirty-First Annual Clinical Congress ended on November 7, 1941, after a successful, though in no way eventful, meeting. There were the usual excellent evening programs on subjects of general or special interest, by men of prominence in their various fields. There were more panel discussions than in previous meetings, and there was one innovation, The Forum on Fundamental Surgical Problems. Daily, organized clinical programs were given by the twenty-eight participating hospitals of greater Boston.

Exactly one month later, the Japanese attack in the Far East gave a new meaning to the 1941 Congress. Few surgeons realize the large number of men who take an active part in such a meeting. Nearly one hundred young men presented the material, and at least two hundred took an active part in the investigative work which was reported in the Forum on Fundamental Surgical Problems. More than one hundred different surgeons contributed to the ever popular panel discussions. The clinical programs in the hospitals were dependent upon the efforts of a majority of the staff members. The special lectures brought widely known surgeons from all parts of the Western hemisphere. In retrospect then, this 1941 Congress assumes a position of importance not recognized during or immediately following the meetings. Not until the present international discord has ended will it again be possible to assemble the man power necessary for a meeting of this proportion.

The Presidential Meeting and Convocation on Monday evening seemed particularly impressive. Symphony Hall, home of the Boston Symphony Orchestra, lends itself unusually well for such an assembly. It was filled with Fellows, their families, and with friends of medicine. The presence on the stage of Temporary Surgeon, Rear Admiral Gordon Gordon-Taylor, of the Royal Navy, of General James C. Magee, Surgeon-General of our own Army, and of Rear Admiral Ross T. McIntire, Surgeon-General of the Navy seemed to anticipate the large number of our new and recent initiates who have since gone into active service in the Army or Navy. It was most appropriate that the President to confer Honorary Fellowship upon Mr. Gordon Gordon-Taylor should be Dr. W. Edward Gallie, a citizen of the British Empire. Mr. Gordon-Taylor's acceptance was brief, sincere, and impressive. His presentation to the College of a bomb shattered relic from the Hunterian Museum brought the tragedy of modern war a little closer to all of us.

The Committee on the Forum on Fundamental Problems, under the chairmanship of Dr. Owen Wangensteen, has successfully established this feature as a permanent part of the program of future meetings, when, once again, young men are available to carry on the investigative work which forms the basis for these reports. The character of these papers and the enthusiasm with which they were received is further evidence of the desire of the Fellows to keep alert to the advances being made in surgery.

The Clinical Pathological Conferences held at the hotel in the latter part of the afternoon, which were organized by Dr. Shields Warren with the help of Drs. Tracy Mallory, Harold G. MacMahon, and Sidney Farber, were extremely popular. Surgical specimens from the various hospitals were collected and projected in natural colors through the Zeiss epidiascope. This material, with a brief clinical history of the patient from whom it was removed, offered excellent teaching material, and it was used to greatest possible advantage.

In previous years, with fewer panel discussions and without the Forum, it was encumbent upon the hospitals to organize a program which would accommodate all of the visiting Fellows. It is quite probable that in future years a better balance may be obtained between hospital and hotel programs than was possible this year. With this in mind, a careful survey of the attendance at the various hospitals has just been completed.

It would not be fitting to make any reference to this meeting without stressing again the spirit of co-operation which existed between the hospitals of metropolitan Boston in the organization and preparation of the clinical program as well as in its final execution. This spirit, which is, in reality, the spirit of medicine, is the basis for the continued success of the College.

Chairman of the Boston Committee on Arrangements.

DEFENSE NEEDS SUGGEST TIMELINESS OF COLLEGE PROGRAM FOR GRADUATE TRAINING IN SURGERY

DALLAS B. PHEMISTER, M.D., F.A.C.S., Chicago, Illinois

At the third Clinical Congress in 1912, the idea of forming the American College of Surgeons was conceived in order to assure that the personnel of the members of the Congress, its clinicians, would represent high moral and ethical standards as well as professional qualifications in the profession. That purpose, then broad and revolutionary, sounds surprisingly narrow now that the original plan and many succeeding ideas have been outgrown in the development of the College. Adaptation and enlargement of its program to meet the current needs have earned for this organization its present authoritative position in directing the advancement of the art and science of surgery through raising the standards of surgical education and practice.

At the moment the activity that best expresses the "outgrowing" or rather "upgrowing" tendency of the College is the program of graduate training in surgery. It has developed quite naturally in connection with Hospital Standardization. The stimulation that it is giving to the creation of more opportunities in more approved hospitals for surgical education is helping to assure our military forces today of surgical service of high quality. It is also aiding our general population to continue having adequate service in civilian hospitals notwithstanding the enlistment of many surgeons in the Army and the Navy. The need for national defense, that includes health defense as a primary requisite, suggests the timeliness of increased effort by the College to provide additional opportunities for adequate training in surgery.

Interruption of training due to enlistment in military service is a problem that existing conditions present. We can ill afford to curtail training for surgery at a time when we urgently need more and better trained surgeons. As a partial solution, certain of the larger general hospitals of the Army and the Navy will probably arrange to provide opportunities for certain junior medical officers to continue their training in these institutions when it is interrupted by enlistment. For those exceptionally well qualified whose training could not be pursued in military hospitals, perhaps exemption or deferment from military service will be obtained. It was the consensus of the Committee on Graduate Training in Surgery held during the last Clinical Congress that in the ensuing year considerable effort should be devoted to the formulation of a definite plan for the solution of this problem. Each recent graduate of medicine having completed his interneship and now having an appointment in a hospital approved for graduate training in surgery should be permitted to continue his training if possible without interruption. The American College of Surgeons can assure the War and Navy Departments that standards of service to hospital patients are always raised when the institution utilizes its resources for professional education. The atmosphere immediately becomes more scientific and more progressive and this reacts to the good of the patient. Difficulties encountered in providing advanced study of the basic medical sciences and research will no doubt be surmounted with the co-operation which may be expected of the medical schools and civilian hospitals. However, the needs of our military forces must be met and under the present world conditions some of our most desirable and ambitious plans may have to be changed.

As for the status of the program in general, it was announced at the 1941 Congress that 216 hospitals, 16 more than the previous year, have acceptable programs for training in general surgery and/or the surgical specialties. Undergraduate teaching is being done in 143 of these approved hospitals. Connections with a medical school provide certain phases of the graduate teaching program in 158 of the institutions approved. Of particular interest is the fact that 41 hospitals without medical school connections are now utilizing their own facilities sufficiently to be included on the approved list. The College recognizes the educational opportunities existing in certain group clinics. Eight of these organizations are included in the present approved list and more are expected to be added from time to time as they develop sufficiently comprehensive programs. As proof that opportunities may be created in different types of hospitals, the 1941 report shows that 109 of the hospitals approved

Chairman of the Committee on Graduate Training in Surgery.

for graduate training in surgery are under community control, 70 under state or municipal ownership and control, 27 under church, 8 are associated with group clinics, and 2 smaller private hospitals now appear on the list.

The 1941 report indicates that there are approximately 1900 men in training in the hospitals approved by the College. The total number of men turned out annually who have completed training of two or more years' duration, in round numbers, is 700. Analysis shows that 60 per cent of these men are receiving training of a duration of three or more years. The effect on surgical standards of releasing each year some 700 surgeons who have had systematic training under good supervision is obvious. It foreshadows the approach of the time visualized from the beginning by the founders of the College when a license to practice medicine would not necessarily be considered as authorization to practice surgery. In the approved hospital, of which there were 2,873 announced at the Congress this year, application of the principles of Hospital Standardization as advocated by the College has exerted a strong influence in confining the practice of surgery to well qualified surgeons. This possibility is being continuously promoted through progress of the program of graduate training in surgery which is operating to insure an increasing number of well trained surgeons each year.

The Committee on Graduate Training in Surgery realizes the importance of continued progress in the work of Hospital Standardization as basic to its own program. No doubt the future of the College and of American surgery is involved in these two important activities of the College. It is through this activity, coupled with the counselorship plan for junior candidates, that the College is projecting itself forward as an influence on the surgery of tomorrow. This it is obligated to do in order to pursue its purpose of continually elevating the standards of the practice of surgery. It also recognizes the stimulation to the younger surgeons which is promoted by the holding of a Forum on Fundamental Surgical Problems in connection with each Clinical Congress. Those who conceived and developed this idea which proved such a popular feature of the Boston meeting are to be congratulated and there is every reason for its repetition. This creation of opportunities to communicate the results of research will focus more interest on the basic science and research aspects of the graduate training program of the College.

In the October, 1941, issue of the College *Bulletin* there were published revised and additional descriptions of approved plans for graduate training in general surgery and the surgical specialties. It was felt that the republication of these plans was justified by the changes wrought in the preceding year and by the intensification of interest in surgical training as a result of the national defense effort. The up-to-date published outlines of these educational programs provide information for the medical student and interne and also an easy method of comparison between institutions. If thereby a wholesome spirit of rivalry is engendered which will lead to the improvement of some of the plans and the inauguration of additional ones, one of the primary purposes of republication will have been accomplished.

The national emergency is placing obvious difficulties in the way of progress, but despite these difficulties the prospects are good for making 1942 a significant year in the annals of surgical education. It is fortunate that the graduate training program is already so far advanced that it can prove its benefits in these critical times when the country is dependent to a greater extent than ever before upon competent surgeons for both military and civilian service.

TWENTY-FOURTH ANNUAL HOSPITAL STANDARDIZATION CONFERENCE

MALCOLM T. MacEACHERN, M.D., Chicago, Illinois

A SPEAKER at the "preparedness" session of the 1941 Hospital Standardization Conference, after mentioning the loss of medical staff members because of their entrance into military service, and the consequent danger of lowering the standards of medical and surgical care of patients, said: "The real difficulty will arise if and when war comes." Thirty-four days later there was no "if" to befog our thinking about preparedness; the United States had been attacked and we were in the war.

The country was at war when the first Hospital Standardization Conference was held in 1917. That fact was a stimulus to the desire to improve hospital service. Said one speaker, "Nearly every hospital epoch, since hospital history began, has been coincident with a war. We are now in the midst of the greatest war that the world has ever known. Then is it too much to predict that we are at the threshold of a new hospital era, one that will witness a marvelous growth in the number of people who seek the hospital when they are sick?"

The prediction has been fully realized. The onset of a greater World War than the first one finds the hospital offering indispensable facilities for the treatment of the sick and wounded. The people have been educated to the value of hospitalization as greatly enhancing their chances for recovery from disease or injury. The war will not change their dependence on the hospital—in fact, will increase it, for, as a discussion leader at the Hospital Conference said:

"Modern warfare with its bombings and casualties of civilian population demands skilled, capable personnel on every hospital staff. . . . We must not make the mistake of the last war by permitting all of the very best men on our staffs to enter military service. . . . Service to the community is just as important as active military duty. . . ."

A shortage of personnel is, however, inevitable. Competent and qualified physicians and nurses, and other trained technical personnel, must be released to the armed forces. The only way to obtain sufficient staffs to carry on in our civilian hospitals is to mobilize all teaching resources for the training of new personnel. As Dr. Bert Caldwell, executive secretary of the American Hospital Association, pointed out at the opening session of the hospital conference, the need is "to train new personnel to replace those called to the colors; to recall into more active service with the hospitals and to retrain the physician and nurse who in years past have staffed them and who by reason of age, disability, or other sufficient cause have been inactive; to place in training an increased number of technical personnel; and to train for civilian service in the care of the sick, men and women who are not accepted for duty with our armed forces."

The defense era was wisely spent by hospitals in planning methods and expedients by which they could continue to give high standards of service when war descended. Many of these were described at the 1941 conference. Recommendations pertaining to personnel included pooling resources among hospitals, for example, one roentgenologist and one pathologist serving several institutions, with technicians being employed to do the detail work. Another suggestion was that surgical specialists be similarly allocated among several hospitals. It was urged that physicians who remain at home take refresher courses in the field in which their interest is greatest, to prepare for more intensive specialization, each man doing the work for which he is best qualified and giving the maximum service. A third very important suggestion was that all staff members be required to attend lectures and demonstrations on the modern methods of caring for emergencies and simple fractures.

A foretaste of the problems that were in store for hospitals was given in the prewar emergency period. During the 1941 survey the field staff of the American College of Surgeons noted that many hospitals, particularly in industrial areas, had an increased volume of work, and were encountering difficulties in carrying the extra load with decreased professional and technical personnel. They found that the services of the medical staff of many hospitals were impaired by a smaller number of conferences to review the clinical work and decreased attendance at conferences, owing to the increased work of physicians. They discovered that some surgeons were using nurses as first assistants at major operations, with the reason given, in some instances, that the regular associate or

Director of Hospital Activities.

assistant was in military service. They reported that the obtaining of adequate medical records was seriously affected by the shortage of internes and residents, and that maintaining adequate nursing service was threatened by the decrease in nursing personnel in many hospitals.

These conditions have interfered considerably in carrying out some of the requirements of Hospital Standardization, but field representatives found that in most instances adjustments were being made to continue to meet the standards. On the whole the performance was remarkably good and augurs well for a creditable war time record. The incentive supplied by the desire for approval by the College promises to be exceedingly helpful in maintaining the quality of hospital service. Administrators say that the public is becoming better informed on ratings of hospitals, and prospective patients frequently ask whether the hospitals in their community are approved. A further factor spurring hospitals to seek and hold approval is the stipulation by many agencies that patronage or aid go only to approved institutions. This is true of state, county, and city governments which subsidize hospitals for the care of indigent patients; of group hospital service plans; of chambers of commerce in endorsing campaigns for funds by local hospitals; of insurance companies when they grant reduced rates on liability insurance; of banks and finance companies in making loans to hospitals; of state boards of nursing education in accrediting schools of nursing; of hospitals accepting affiliate students for special courses in nursing; of the American Red Cross in its extension program of volunteer workers; and of federal and state governmental departments charged with the granting of funds for indigent crippled children's care. It will doubtless also apply to aid extended by the federal government for financing additions to physical plants and for meeting the expense of training certain types of personnel. All of these agencies show by their use of it that the gauge of approval is a valued help to them in determining which hospitals merit their assistance.

In the first World War, the War Department lacked a reliable means of judging the competence of physicians, particularly specialists; consequently many men were misplaced—as one surgeon expressed it, there were numerous "round pegs in square holes." Now that hospitals are standardized, and their medical staffs are organized, it should be possible to ascertain directly from his hospital what standing the individual physician has in medicine, surgery, or a specialty. The College and other medical organizations also now have complete information concerning their members. It is essential that during the war period the requirements of the College concerning appointments to, and organization and control of, the medical staff be met as usual, with a minimum of tolerance of practice outside the designated field, in case of necessity only.

An interesting feature of the 1941 Hospital Standardization Conference was a series of panel discussions on the obstetrical department, the department of orthopedic surgery, the department of anesthesia, the department of ophthalmology and otolaryngology, and the department of urology, respectively. The discussion covered the essentials pertaining to efficient operation of these departments, and included consideration of education and training of the various specialists.

The 1941 list of approved hospitals, as announced at the Hospital Standardization Conference, showed 2,526 institutions fully approved, 347 provisionally approved, a total of 2,873. The total number of hospitals under survey in 1941 was 3,688, of which 77.9 per cent were approved. With the country at war, it is especially encouraging to have so many military and civilian hospitals which are organized and equipped to afford the physician the greatest possible assistance in his endeavor to save life and minimize suffering and disability from illness and injury. This year it is planned to promote the standardization of those Army hospitals which have not been approved, owing to the fact that it has not yet been possible to survey them. Last fall in continental United States there were 218 Army hospitals with a total bed capacity of 79,019, which is rapidly growing.

The need now is to view our hospital situation as a whole, with due consideration for safeguarding both military personnel and civilians. We face total war, which means total hospital service. Our 24 years' work in active encouragement of the improvement of hospitals is yielding high returns today in preparedness to meet the needs of America at war. Unrelaxing effort to keep the standards high will bring us through the conflict with a brilliant record of service by our great modern hospitals and the personnel that they have trained.

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Massachusetts General Hospital—Arthur W. Allen
Massachusetts Memorial Hospitals—Frank E. Barton
New England Baptist Hospital—N. W. Swinton
New England Deaconess Hospital—B. P. Colcock
New England Hospital for Women and Children—L. D. Adams
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The Thirty-second Annual Clinical Congress of the American College of Surgeons will be held in Chicago, October 19–23, 1942.

CLINICAL CONGRESS TECHNICAL EXHIBITION

LEADING manufacturers of and dealers in surgical instruments, hospital apparatus and supplies, diagnostic and therapeutic apparatus, pharmaceuticals, and publishers of medical and surgical books were represented in the Technical Exhibition at the Hotel Statler in Boston, November 3–7, 1941.

W. D. Allison Co., Indianapolis
A. S. Aloe Co., St. Louis
American Cystoscope Makers, Inc., New York
American Hospital Supply Corp., Chicago
American Safety Razor Corp., Brooklyn
American Sterilizer Co., Erie, Pa.
D. Appleton-Century Co., New York
Armour Laboratories, Chicago
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C. R. Bard, Inc., New York
Bard-Parker Co., Danbury, Conn.
W. A. Baum Co., Inc., New York
Baxter Laboratories, Glenview, Ill.
Rudolph Beaver, Inc., Waltham, Mass.
Becton, Dickinson & Co., Rutherford, N. J.
Julius Berbecker & Sons, New York
Burdick Corp., Milton, Wis.
S. H. Camp & Co., Jackson, Mich.
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Warren E. Collins, Inc., Boston
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Cutter Laboratories, Berkeley, California
Davis & Geck, Inc., Brooklyn
J. A. Deknatel & Son, Queens Village, N. Y.
DePuy Manufacturing Co., Warsaw, Ind.
A. W. Diack, Detroit
Duke Laboratories, Inc., Stamford, Conn.
Eastman Kodak Co., Rochester, N. Y.
J. H. Emerson Co., Cambridge, Mass.
Foregger Co., New York
General Electric X-Ray Corp., Chicago
High Tension Electric Corp., New York
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E. R. Squibb & Sons, New York
Surgery, Gynecology and Obstetrics, Chicago
Taylor Instrument Cos., Rochester, N. Y.
Charles C. Thomas, Springfield, Ill.
Tower Co., Seattle, Wash.
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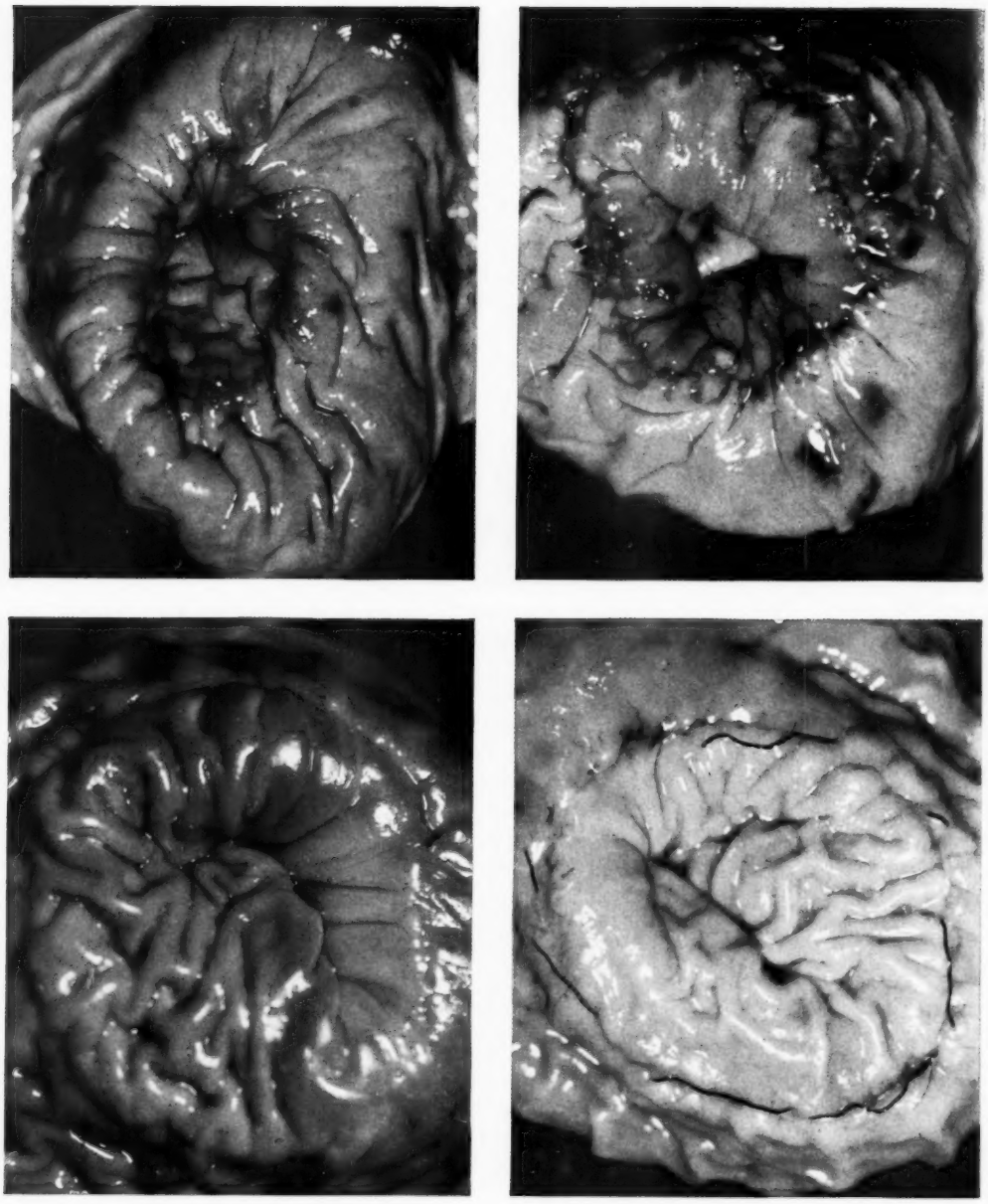

Figs. 1 and 2, above—two days
Figs. 3 and 4, below—seven days

The Superiority of Fine Catgut over Fine Silk as a Mucosal Suture in Gastric Surgery.—John O. Bower and A. E. Pearce.

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